THE ECZEMAS

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A SYMPOSIUM BY TEN AUTHORS

Edited by

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PREFACE

ECZEMA of one kind or another is so common that it ranks high among the causes of morbidity both in peace and war. Its understanding and management concern not only the dermatologist but the general practitioner, the paediatrician, the allergist and other specialists; hence this symposium has been planned to include material of interest to all these. Much recent research is presented here by some of the leading workers and should help to remove the unjust stigma of empiricism from dermatology. I have tried, nevertheless, to keep in mind the needs of the general practitioner who prefers a practical guide rather than a maze of argument; it is inevitable that in these circumstances some bias will be shown, but at least he will find a straightforward account with no important internal contradictions.

Many will no doubt deplore the absence of a chapter on psychosomatic influences. These are briefly touched on in various parts of the text, but are not given the prominence which is accorded them by some schools. In my opinion, this subject is not yet sufficiently advanced to warrant its inclusion on an equal footing with the scientific studies presented here. We know from history how a troubled world turns for comfort to the supernatural. Is it only a coincidence that psychosomatic studies have recently gained such prominence? This is not to say that such investigations are barren; on the contrary, they should be pursued with vigour and enthusiasm, provided that conclusions are subject to the laws of scientific proof which are demanded in every other branch of Medicine.

The foregoing are, of course, my personal views; similar responsibility attaches to the wording of Chapters VI and VII, which I translated from the original German.

It is with a deep sense of obligation that I record my thanks to my fellow contributors, whose work forms the main part of this book. Their ready participation in the project and their eagerness to help throughout have indeed made my task a light one. In particular, it is my pleasant duty to thank Dr. G. A. Grant Peterkin, who so willingly and efficiently undertook not only the selection and incorporation of the coloured illustrations but also a host of editorial tasks and responsibilities which for geographical reasons were beyond my powers. Dr. Marion B. Sulzberger was among the first to support the project and gave generously of his time and

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experience when I needed advice His first words—" keep it short —are only one of the many hints for which the reader should share my gratitude

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1954

CHAPTER I

INTRODUCTION CLASSIFICATION MORPHOLOGY

L. J A. LOEWENTHAL

THE confusion surrounding the eczemas is too well known to need elaboration. Traditional teaching does not stress the essential similarities and differences of the various members of this group of diseases, nor their tendency to accompany or succeed each other Text books are also apt to place these varieties in compartments, often separated by sections of other material The student, practitioner and younger dermatologist see the eczemas as a bewildering mass of imperfectly defined entities, without logical arrangement, orderly approach or rational scheme of treatment.

Our first object therefore, is to integrate available facts and theories so as to present this group of skin diseases as a whole; the second is to arrange them in a classification which, though imperfect, will at least provide a framework around which items of knowledge can be built. Our third object is to make generally available some of the important modern work on the pathogenesis of the eczemas; much of this fundamental research is still missing from the text books although its understanding should be regarded as essential to the student of dermatology It will be shown that such Laboratory studies have a *direct practical bearing* on the diagnosis, and hence the practical management of the eczemas. Though it is hoped that this work will provide a convenient starting point for those who are interested in further research our principal object is to present the clinical worker with a comprehensive account of the eczemas.

DEFINITION

Eczema is not a disease. It is a group of physical signs, the evidence of an inflammatory reaction of a special kind. It exhibits the cardinal signs of inflammation—heat redness, swelling and

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DEFINITION

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itching, the last representing a pain equivalent As these changes are brought about by influences of the most diverse kind, from outside the body or from within no useful purpose can be served by trying further to define a hypothetical disease Eczema "

Historically we find that the word originally meaning a "boiling over" has been used in different senses at various times. Hebra[1] was the first to combine in an orderly way Willan's description of eczema as a non-contagious eruption of small closely-set vesicles with the teaching of Rayer[2] and his followers who broadened the concept of the disease process, but even he was compelled to define it solely by description After almost a hundred years we cannot go much further in the matter of definition. There is a series of naked eye and histological changes which taken together constitute an eczema These will be described in the course of this work, where the various causative factors, known or suspected will be examined

TERMINOLOGY

The introduction of the word "dermatitis" has done nothing to clarify the concept of eczema Rather has it led to further confusion for different schools use the word to denote different conditions. Thus "eczema" implies an endogenous condition in England and a reaction to external noxae in Germany and the word dermatitis" is, in England inseparably connected with industrial skin disease. In the United States "atopic eczema and "atopic dermatitis have been used by different authors to denote the same disease.

This work is not planned to perpetuate any supposed distinction *between these terms* and contributors will use whichever they think more suitable; the reader may rest assured that in these pages, they may be regarded as equivalent. Clarity follows, not the selection of one term or the other but the use of an explanatory adjective such as "contact, "seborrhoeic" or "atopic" That this simplification is essential may be gathered from any dermatological discussion of the subject Linn has recently enumerated the various meanings applied to "eczema" and "dermatitis" in the English-speaking world alone and demonstrated the absurd confusion into which these terminological battles can lead us

Substitution of terms such as *épidermite* and *dermo-épidermite* " is an attempt to focus attention on the affected tissue; though more precise than the word eczema" they do not help

us towards a clearer concept. The coming of new names has, in most cases, made the understanding of the eczemas still more difficult. Although an attempt will be made in this work to add synonyms, it must be realised that such terms are not always co-extensive. Thus a recent text book uses the term "dermatitis venenata" to denote what we call "primary irritant dermatitis" another originating in the same country uses it also to include what we call "eczematous contact-type dermatitis" or more simply "contact eczema" These problems in nomenclature are not of mere academic interest; so long as they exist they place an additional and unnecessary obstacle in the way of understanding the eczemas. International agreement in this matter is long overdue.

The word *eczematoid*" has been used in different senses; it is perhaps best employed to describe eruptions which resemble eczema but lack one or more of the essential criteria It will usually be found to mean an absence of intra-epidermal vesiculation this process customarily being regarded as a cardinal sign of eczematous, as distinct from other types of dermatitis.

MORPHOLOGY

Uncomplicated eczema usually presents different stages of evolution simultaneously It used to be accepted that various kinds of eczema papular vesicular pustular and others, deserved individual description; that this is not so was first clearly shown by Hebra He took careful note of the evolution and appearance of lesions produced by one or more applications of croton oil to various parts of the body: this primary irritant dermatitis or as he called it, artificial eczema," does in fact reproduce all the subjective symptoms and naked eye changes shown at various times by eczemas of any kind. To enumerate them briefly —

Itching is a constant and early feature in most cases. Objectively there is initial *redness* succeeded by the development of one or more of the following signs.

Vesicles are often regarded as the typical lesion of eczema but their presence is not considered essential by most authorities, at least in a form visible to the naked eye. As will be shown later they tend to appear more profusely on certain areas and in response to stronger stimuli. Thus Hebra found that further applications of croton oil on an already eczematous site produced more vesiculation (Fig. 1)

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Papules are seen chiefly in areas where vesicles do not readily form and in more chronic eruptions. They may also represent a stage in the development of vesicles. In widespread eczemas there is always a distinct tendency for vesicles and papules to form more or less regular groups while discrete lesions are scattered elsewhere.

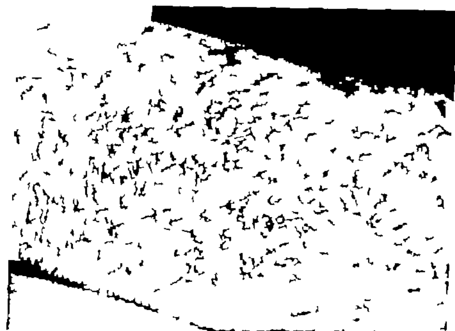


FIG. 1
Vesicular eruption produced by a primary irritant—40 per cent commercial formaldehyde

Oedema is particularly evident where the skin is not firmly bound to subcutaneous tissue and is therefore commonly seen when the eyelids and genitalia are affected it may however be detected *in any area by the brawny feel of the lesions.*

Scaling on an Erythematous Base may be the only manifestation of an eczema or it may represent a stage in the subsidence of other *forms In the former case it illustrates the parakeratotic eczema* of some French authors, the *eczématides* of Darier the dry forms of seborrhoeic eczema eczematoid dermatitis *and many other* conditions which have no claim to special titles (Fig 2) It is noteworthy that Hebra mentioned this variety as one of the possible *forms of reaction to croton oil* without intermediate papular or vesicular stages. In spite of the fact that it may form part of the picture *of many* different types of eczema the red, scaly lesion is

most frequently and typically seen in cases with microbial causation. Chapter V makes it clear that there is no sharp distinction histologically between these and other varieties of eczema.

Secondary Changes. Few eczemas clear without at some time weeping; in the distant past, indeed, a "true eczema" was not



FIG. 2

Erythemato-squamous eczema of bacterial causation. Dorsum of foot.

accepted unless rupture of the vesicles had led to a raw oozing surface in which minute depressions—the pits of Devergie—could be seen. Other sequelae are shown in Figure 3 they are usually the result of infection or prolonged scratching.

Experience shows that the sequence set out in this diagram *may occur in any form of eczema* and is not peculiar to the primary irritant dermatitis of Hebra's experiment. The process may of course, be arrested at any stage from erythema onwards, and lichenification is only a possible, not inevitable, result (Fig. 4) It is common to find more than one type of lesion at any given time: thus a patient with extensive eczema may present crusted and lichenified lesions of the hands and wrists, groups of papules and vesicles on the arms, and denuded, weeping axillae (Fig. 5)

Pigmentation and Loss of Pigment are non-specific changes which may follow any inflammatory affection of the skin; it is not, therefore, surprising that either may be seen in many varieties of eczema.

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The Nails. Any eruption involving the nail folds is apt to produce corresponding changes in the nails; distortion, especially a transverse corrugation, may therefore be a sign of previous eczematous involvement of the fingers.



FIG. 5
Crusted and lichenified eczema.

ALLERGY AND THE ECZEMAS

The subject to be considered here is so vast that no more than a few generalizations can be attempted. More detailed information will be found in other chapters, but it is desirable to preface these with a brief introduction. If a more thorough approach is needed, the reader is advised to consult the references appended to this and succeeding chapters.

The word "allergy" has become so misused that its frequent employment in relation to the eczemas is becoming a handicap rather than a help in understanding them. Such statements as "This patient has an allergic eczema" or "Do you think I am allergic?" are in constant use; unless qualified they add nothing to and detract much from the intelligent appreciation of a case. "Allergy" is a euphonious word, its employment is calculated to clothe the most jejune diagnosis with a cloak of scientific respectability. The tendency to be satisfied with allergy as a diagnosis, instead of an indication for further highly specialized enquiry is

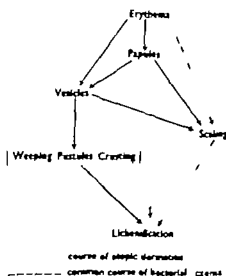


Fig. 3

Diagrammatic presentation of the possible course of any eczema.



Fig. 4

Erythema, papules nd lichenification in third week of universal eczematous outbreak

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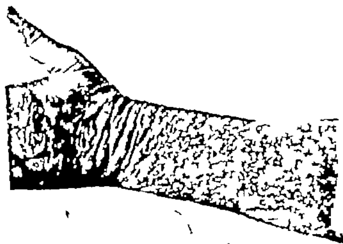


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to be deplored it commonly results in the employment of unsuitabl tests and a squandering of anti-histaminic drugs And yet our knowledge of the eczemas incomplete though it may be, owes almost everything to the concept of allergy just as our knowledge of allergy is based to a great extent on the study of eczema

Allergy has been defined by Sulzberger[1] as *any specifically acquired alteration in the capacity to react* Further "the term specifically here refers to the fact that the alteration in capacity to react results from exposure to an exciting agent and is not universal but is made manifest upon re-exposure only to the same or an immunologically related agent"

Though by definition it includes a diminished capacity to react (hypoergy or anergy) it will usually be found in this work to imply the commonly accepted if incorrect, meaning of an increased capacity to react.

TYPES OF CUTANEOUS ALLERGY

A primary classification according to the site of the shock tissue is useful as an introduction though modern work (*see* Chapter III) suggests that such differentiation may not be scientifically valid.

The Eczematous Response is the first type to be considered here the epidermis is regarded as the shock tissue and the reaction becomes fully developed in twenty four to forty-eight hours This reaction is described as ECZEMATOUS DERMATITIS or simply ECZEMA, and is characterized by certain typical histological findings commonly regarded as originating in the epidermis (Chapter V) This response is seen in varying degree in all but one of the conditions considered in this work unless the exception (atopic dermatitis) is specifically named, therefore future remarks on allergy and eczema may be taken to refer to eczematous dermatitis

The Urticarial Response is the other allergic type commonly seen in the skin Here the cutaneous blood vessels form the shock tissue and the reaction manifests itself by the IMMEDIATE formation of a wheal ATOPIC DERMATITIS considered fully in Chapter IV is regarded as belonging to this group In this condition changes in the epidermis at least after infancy are regarded as secondary and the intra-epidermal vesicle of eczematous dermatitis is not seen typically

There are fundamental differences between eczematous and atopic dermatitis; the distinction must be realized before further

classification is undertaken. The salient distinguishing features are conveniently summarized in Table 1 (page 76)

It is as well to bear in mind that reactions to be classified as allergic must be specific, and that sensitivity elicited on first exposure to a substance, or by non-specific traumata such as heat or friction, should not be called allergic. Thus, at the outset, we see that all apparently eczematous reactions are not necessarily allergic: Hebra's croton oil experiment, for instance, does not depend on a specifically acquired property for the first and all subsequent exposures produce the effect. In order to decide that an eczema is of allergic nature certain conditions must be present:—

1 The causal agent, or allergen, must have been encountered previously

2. A latent or "incubation" period of at least four days must elapse before the state of sensitivity manifests itself

3 The eczematous reaction occurs only after a subsequent exposure. This exposure need not necessarily be the second, in fact many years of constant exposure may elapse before the eczema reaction appears.

An apparent exception to the above conditions is seen in the phenomenon of "spontaneous flare-up" Here a single and first application of an allergen may after an interval of five or more days, produce an eczematous reaction at the site of application. This is best explained by assuming that traces of the allergen still remain at the site of application when sufficient time has elapsed for sensitivity to develop. In other words, there has been a continuous application for five or more days in place of successive applications with an intervening incubation period.

A fact of fundamental importance remains to be stated, that *the whole skin becomes sensitized simultaneously* although only a limited area has been in contact with the first, or sensitizing, application. The technique of patch testing and the mechanism of dissemination of eczema are only two of the important subjects which depend on the *recognition of this fact*. Haxthausen who has done much of the recent work, discusses this phenomenon more fully in Chapter III It is customary for text books of dermatology to begin with a statement such as: "The skin is an organ only too rarely is this statement amplified Yet in considering the eczemas it is imperative to realize that the whole

It must be stated, however that this type of primary irritant dermatitis, though eczematous in appearance, does not fulfil the *histological* criteria of eczematous dermatitis.

skin does behave as one organ and that the understanding of contact eczema and its complications depends on this fact.

CLASSIFICATION

Attempts to classify eczematous dermatitis into exogenous and endogenous varieties have been made, but a little reflection shows that often no clear-cut distinction is possible. Thus the sensitizing exposure may take place through the blood stream, after ingestion or injection of the allergen and the eliciting exposure by superficial contact. Quinine and mercury provide two examples of this mechanism they are frequently ingested for therapeutic reasons (sensitizing exposure) and frequently applied to the skin surface, for example as ingredients of sun-screening or antiseptic ointments (eliciting exposure) The converse is also seen. the first topical application of a sulphonamide (sensitizing exposure) produces no reaction but after an interval of a few days to several years the ingestion of sulphonamide tablets may be followed by an eczematous reaction at the site of the original application (eliciting exposure) As will be seen in Chapter VII a similar mechanism is also likely in cases regarded as eczema produced by bacteria

It has been stated that the disease called atopic dermatitis can be sharply differentiated from all other eczemas. It is the only condition described in this work in which a family or personal history of other allergic manifestations is relevant In classification therefore, as in diagnosis and management, it is to be considered as an entity having no relationship to any other eczematous or eczematoid dermatitis.

Of the other conditions which we are to consider the macroscopic and histological features may vary in type and degree; but there is a considerable amount of overlapping and on the whole their resemblances are more striking than their differences The classification which follows is therefore based principally on causation and to a lesser degree on features regarded as characteristic of the development of the various types. It is thus an essentially practical arrangement attempts at classifying the eczemas on more scientific grounds cannot at present succeed, in view of the considerable gaps that still exist in our knowledge of aetiology

I Atopic Dermatitis

This is fully considered in Chapter IV

2. Primary Irritant Dermatitis

This may be defined as a reaction simulating eczema which is produced in the normal skin by an irritant acting in sufficient concentration for a sufficient time. It is produced at the first and all subsequent applications and *no allergic mechanism is involved in its production*. Croton oil already referred to is an example of such a primary irritant, as are mustard, certain inorganic acids, and many other substances. The reaction produced by primary irritants is sometimes called "toxic" some of the contributors to this work use the term in this sense.

In this group we must also include eczemas which arise from minor traumata in an abnormal skin; the changes in skin metabolism described in Chapter VI are particularly relevant here, for in their presence such relatively harmless substances as soap take on the character of primary irritants. Generally speaking, however a primary irritant is taken to mean a substance which under standard conditions, produces an eczema reaction on the majority of normal skins.

3 Eczema from Physical Causes

The changes produced by acute sunburn provide a familiar example. An eczematous reaction can usually be elicited in any skin (except that of the healthy Negro) by exposure to natural sunlight or ultra-violet rays, after a length of time depending on the degree of pre-existing pigmentation. This phenomenon should probably be classed as a primary irritant dermatitis; but in certain cases a hypersensitivity may be *acquired* and in such cases the resulting eczema more probably represents an allergic reaction. The matter is further complicated by the fact that certain substances may sensitize the skin to sunlight, though not themselves provoking an allergic reaction when light is excluded, as, for example, under conditions of patch testing. Among these substances are included such photosensitizers as tar and certain vegetable juices, as well as endogenous products such as porphyrins.

4 Eczematous Contact Dermatitis

The term "Contact Eczema" may be conveniently applied to this condition, though some authorities (*e.g.* Bettley in Chapter II) also use it to include certain types referred to above as Primary Irritant Dermatitis. Eczematous contact dermatitis provides the best example of the effects of specific allergic hypersensitivity Here

skin does behave as one organ and that the understanding of contact eczema and its complications depends on this fact

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Attempts to classify eczematous dermatitis into exogenous and endogenous varieties have been made, but a little reflection shows that often no clear-cut distinction is possible Thus the sensitizing exposure may take place through the blood stream after ingestion or injection of the allergen and the eliciting exposure by superficial contact. Quinine and mercury provide two examples of this mechanism they are frequently ingested for therapeutic reasons (sensitizing exposure) and frequently applied to the skin surface, for example as ingredients of sun-screening or antiseptic ointments (eliciting exposure) The converse is also seen. *the first topical* application of a sulphonamide (sensitizing exposure) produces no *reaction but after an interval of a few days to several years the* ingestion of sulphonamide tablets may be followed by an *eczematous reaction at the site of the original application (eliciting* exposure) As will be seen in Chapter VII a similar mechanism is also likely in cases regarded as eczema produced by *bacteria*

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I ATOPIC DERMATITIS

This is fully considered in Chapter IV

focus, examples of widespread non-atopic eczema are rare. They are called "endogenous" because it is surmised that some internal cause must be operative and because a word of Greek derivation is more palatable than a mere confession of ignorance in a modern language Where there is no certain knowledge it is apparently permissible to speculate hence the "humours" of our great grandfathers appear again in the guise of "metabolites," "neuro-vegetative-humoral influences" and "psychosomatic manifestations. The subject is considered more fully in Chapter IX.

8 NUMMULAR ECZEMA

This is regarded by many as a distinct entity It must be admitted that a number of cases show a similar pattern in the development and course of the lesions called by this name, and in these the most careful investigation may fail to reveal the cause The status of nummular eczema is discussed more fully in Chapter X, the section which follows (Reaction Patterns) points out one objection to using this term as a diagnostic label

9 MIXED TYPES

It is generally agreed that a combination of atopic and seborrhoeic dermatitis is not uncommon (Chapters IV and VIII) but there is no evidence that either condition predisposes to the other Some of the other types of eczema, however show a decided tendency to complicate each other and careful study of advanced cases often enables us to deduce the succession of events, which often follow one of these four patterns:—

Contact eczema→bacterial eczema→dissemination.
Alkali eczema→contact and/or bacterial eczema→dissemination.
Eczema from dermatophytes→bacterial eczema→dissemination.
Eczema from dermatophytes→contact eczema from over-treatment→dissemination.

Other combinations are seen, and the intermediate stage of bacterial eczema is apparently not essential. Appreciating these forms of progression is of great help both in diagnosis and treatment.

REACTION PATTERNS

THE MORPHE

It has been stated, and cannot be too often emphasized, that the eczema reaction may go through any of the stages shown in Figure 3 Further two or more of the elementary lesions frequently combine to form more complicated pictures. In this way plaques

the skin reacts to the presence of one or more substances with which it is brought in contact in strict accordance with the criteria set out above in the section "Allergy and the Eczemas." Contact eczema is of common occurrence and by nature it is eminently suitable for observation and investigation It therefore forms the subject of the next two chapters and provides a logical starting point for the consideration of other (but not atopic) forms of eczema.

5 Microbial Eczema

Contact eczema is produced by chemical substances often of a relatively simple nature many authors contend that microbial eczema is an essentially similar reaction to the products of living organisms and in fact, that it is merely contact eczema of a particular kind Observations and experimental work including that described in Chapter VII lend weight to this contention Such phenomena as the sudden outbreak of papular and vesicular eczema in areas contaminated by infected discharges have long been called "infectious eczematoid dermatitis" (Chapter V) the clinical and histological appearances of infection of the glabrous skin with dermatophytes also justify the use of such terms as "eczematous" or "eczematoid ringworm"

Seborrhoeic Dermatitis may likewise be regarded as a microbial eczema of a special kind but, as Peterkin points out in Chapter VIII unknown constitutional factors play a large, or even decisive part in its aetiology

6 Disseminated Eczema

This term will be used to designate the appearance of more or less extensive, symmetrical areas of eczema at a distance from one or more primary foci It is the commonest variety of extensive, non-atopic eczema and may complicate a local eczema of any type, or even certain non-eczematous eruptions. Its relationship or possible identity with the "id" eruptions of bacterial and fungous origin and with the phenomenon of autosensitization is discussed at length in Chapters III VII and IX It is of the greatest theoretical interest and of the highest importance in the diagnosis and management of the eczemas

7 Endogenous Eczema

Except for such cases as are demonstrably caused by allergy to drugs or foods or are the result of dissemination from a primary



FIG. 8
Nummular lesions showing surrounding areola and satellites.



FIG. 9 FIG. 10

FIG. 9.—Nummular lesion with crusting and scaling.
FIG. 10.—Nummular lesion with central clearing and peripheral crusting; final stage.



FIG. 6

Early stage in development of nummular lesion. Disseminated eczema from a primary focus on the other leg.



FIG 7

Second stage in development of umm lar lesion Not central clearing. D sseminated eczema *from contact eczema caused by shoe le ther*

The converse is also true: lesions with the same causation may at different times and in different subjects present dissimilar appearances. Those who have had experience of contact eczema in industry will recall how varied are the responses elicited in different subjects by comparable exposures to identical allergens. Even in the same patient the same noxa often produces lesions which differ morphologically in various areas; Hebra's observation of this fact has already been mentioned.



FIG. 12
Papulo lichenoid lesions in a Negro. This disseminated eczema developed only one week previously

Three important generalizations may now be stated.—

1 *Any variety of eczema may produce a diversity of lesions*

2 *Any type of eczematous lesion can be produced by any of the aetiological varieties of eczema,* though some of these commonly present a distinct pattern. It follows that

3 *Inspection alone cannot determine the cause of an eczematous lesion* (see Fig. 11)

At this stage it is desirable to examine the factors which are known to influence the morphe of eczematous lesions.

1 **Individual and Racial Peculiarities.** A skin which is naturally dry either congenitally or through age or any other reason does not produce vesicles as readily as does one of normal texture. Again, even when the texture of the skin is apparently normal,

are often formed consisting of an erythematous base, with or without visible oedema on whose surface papules and vesicles may be studded Adamson regarded these as the essential lesion of eczema and stressed that, when these areas are pinched up between the finger and thumb they are found to have two or three times the thickness of normal skin These nummular patches show many



Fig. 11
Reaction to sulphur ointment. Inspection suggests the diagnosis of seborrhoeic dermatitis.

variations some tending to central clearing with scaling others preserving their papules or vesicles over the whole surface Some again have a sharply demarcated edge; others show a surrounding areola which fades insensibly into normal skin still others show satellite lesions outside their borders (Figs 6 to 10) It would be *absurd to label "nummular eczema" all varieties which show the* above forms for in addition to the disease which we call by this title bacterial and fungous infections as well as disseminated and endogenous eczemas can produce these lesions. Indeed we have only to remember that the disease we call nummular eczema bears the inaccurate synonym of "parasitic eczema and in addition is among the dermatoses most commonly confused with contact eczema.

may be seen. Vesicles, for example, tend to be larger where the skin normally has a thicker horny layer on the extensor surfaces of the limbs and especially on the palms and soles, where confluence of vesicles may produce a lake of exudate under the unyielding *stratum corneum*. It is thus usual to see large, even bullous lesions on the palmar surface along with pin-head sized vesicles on the sides of the fingers. This condition, cheiropompholyx, is therefore simply a manifestation of eczema at least in the majority of cases, as was long ago pointed out by Wise and Sulzberger

Erythema is present in all locations but the subsequent type of eruptive elements in different areas is frequently as follows:—

SCALP scaling, weeping, crusting. No vesicles.

EYELIDS: scaling. Vesicles rarely

ELBOW and knee flexures: papules.

PALMS AND SOLES. vesicles and bullae almost always. Scaling common. The erythema may be masked by tension from the oedema.

Lichenification, which is always the result of prolonged rubbing or scratching, will naturally appear most often in areas that are most accessible to the fingers. There is little doubt, too that certain persons skins lichenify more readily than others

5 **Type of Allergen.** Eczemas caused by surface bacteria are not commonly vesicular sharply marginated patches of redness with scaling are most typically seen and these may be modified by their situation and appear in the flexures as raw oozing areas. *These appearances have for many years been associated also with the concept of seborrhoeic dermatitis* Chemical allergens show no difference among themselves in the type of contact reaction produced, except in so far as the intensity of the reaction is concerned. Nickel forms the sole exception, and is referred to in Chapters II and IV

THE DISTRIBUTION

Just as certain types of lesion appear again and again in patients suffering from eczemas of widely different aetiology so certain patterns of distribution become familiar through constant repetition. The feeling that such patterns must point to an identity of cause has been responsible for much confusion; one still reads of flexural eczemas automatically being regarded as "neurodermatitis" (*i.e* atopic) when the only reason for this view is the site of the eruption. It may therefore be stated that *the distribution pattern alone is not*

variations in reaction are common, this is well exemplified in the Negro skin where a lichenoid reaction is seen as the commonest of the lesions produced by eczema (Fig. 12) There is some evidence that such differences in the morphe of reaction cannot be attributed solely to varying degrees of sensitivity



FIG 13
Contact eczema, with bullous lesions, appearing after one week's application of a sulphonamide ointment for insect bites. Infant aged 10 months.

2. **Age.** Vesicles and bullae form more readily in children than in adults (Fig 13) *This fact is of importance in atopic dermatitis,* where vesicles are seen in the very young, while their absence constitutes an important diagnostic feature in the adult (Chapter IV)

3 **Intensity of Reaction.** If simultaneous patch tests be made with serial dilutions of a substance to which the subject is allergic *a range of eczema responses can be demonstrated the weakest* reaction is a simple erythema a slightly stronger one will produce visible or palpable oedema as well and higher concentrations will in turn evoke *papular vesicular and bullous lesions The most* violent reaction will produce in addition eczematous lesions out side the area of contact A similar gradation of changes can be *seen after applying a given* concentration of allergen for increasing periods of time

4 **Site.** Hebra s experiment showed that different areas tended to react in *different ways though exceptions* to the common trend

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4 **Site** Hebra's experiment showed that different areas tended to react in different ways *though exceptions to the common trend*

suggest specific types of eczema, a final and incontrovertible aetiological diagnosis cannot be made only by inspection. To achieve this no amount of visual acuity can take the place of a careful history and intelligently directed investigation

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Although many departures from the main types are seen and many cases exhibit a combination of more than one pattern three distributions are sufficiently characteristic to deserve description. They are here named after the diseases which typically exhibit the appropriate patterns· *no aetiological relationship is suggested*

1 **The "Atopic" Pattern.** In this the eyelids, sides of the neck upper chest, elbow and knee flexures are predominantly affected When the eruption spreads from the neck to involve the upper chest it typically produces a U-shaped area of eczema quite unlike the V" pattern of most cases of solar dermatitis.

2. **The "Dermatitis Herpetiformis" Pattern.** The scapular and gluteal regions, forearms and legs are typically affected.

3 **The "Nummular Eczema" Pattern.** This is similar to the previous type but also and most typically involves the backs of the ngers and hands, the upper arms and thighs. Curiously nough the lesions themselves tend to a nummular morphe when this distribution is picked out, irrespective of the type of eczema

SUMMARY

Eczema now emerges as a cutaneous manifestation of irritability It can be provoked by the presence in or on the skin of various substances living or dead, organic or inorganic, tangible or radi ated. The reaction usually represents an allergic tissue response but primary irritation can cause a clinically similar train of events without an allergic mechanism taking part

In cases where the causative substances reach the skin from within, eczema must be sharply differentiated into atopic and non atopic· the latter group includes the secondary disseminated eczemas which follow a local lesion as well as those which are caused by drugs foods, foci of infection or other unknown and debatable stimuli

Irrespective of the type of eczema in any particular instance both the morphe and distribution of the lesions follow a limited number of patterns and although certain clinical pictures may

suggest specific types of eczema a final and incontrovertible aetiological diagnosis cannot be made only by inspection. To achieve this no amount of visual acuity can take the place of a careful history and intelligently directed investigation.

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Irrespective of the type of eczema in any particular instance both the morphe and distribution of the lesions follow a limited number of patterns and although certain clinical pictures may

are also in this category for example rubber or the chemicals used in processing it, plastics and paraphenylendiamine. The acridine antiseptics, sulphonamides and some antibiotics have marked sensitizing properties though they are not often manifest unless they are applied to the skin of which the corneous layer is already deficient or damaged by some other agent.



FIG 14
Acute vesicular eczema of the forearms of few days duration resulting from the application of sulphonamide cream to which the patient was sensitive. Numerous closely-set vesicles, some coalescing to form bullae

The degree of sensitivity in these cases is often very high. In a case of my own sensitivity to benzthiazole gave positive patch tests at a dilution of 1 in 10 and in another case sensitivity to amethocaine gave positive tests at a dilution of 1 in 10

Clinical Features. This type of eczema, especially in its acute form, is characterized objectively by bright red erythema followed by closely-set superficial clear polygonal vesicles varying in size and commonly two or three millimetres across (Fig. 14) Subcutaneous oedema is usually more marked in this type of eczema

CHAPTER II

CONTACT ECZEMA SOME CLINICAL CONSIDERATIONS

F RAY BETTLEY

THE fuller recognition of the part played by epidermal contact sensitivity in the causation of eczematous eruptions has constituted perhaps the greatest advance in clinical dermatology in recent years It is a clinical field which is still extending and of which much remains unexplored

It is often useful to think of eczemas in regard to this sole criterion of epidermal contact sensitivity and to attempt to classify them accordingly When this is done contact eczema with a high degree of epidermal sensitivity represents the simplest indisputable example in which no other factor is likely to be of great importance. At the other end of the extreme may be placed the type often known as discoid or nummular eczema in which epidermal sensitivity to external contacts plays little or no part and which indeed is comparatively seldom even exacerbated by external factors. According to this criterion of contact sensitivity cases of eczema may be roughly grouped into a consistent and useful classification

1 CONTACT ECZEMA WITH SPECIFIC ALLERGIC EPIDERMAL HYPERSENSITIVITY

The simplest example of this type of eczema is the positive patch test with vesicular response obtained by the application of a non irritant substance in a hypersensitive subject. In this type of sensitivity the allergen is not a primary irritant *i.e* has no apparent effect on the skin of a normal person in whatever concentration it is applied although it may have a considerable tendency to sensitize Allergens of this kind may occur naturally and allergies to plants are often of this nature sensitivity to primula chrysanthemum or poison ivy is of this type. A considerable number of synthetic substances used either as drugs or otherwise

Very often, in such a case, the face, especially the eyelids, are the worst affected, and the hands, with their thicker corneous layer relatively spared.

The time relations of this type of contact eczema are similarly comparatively clear-cut. In a sensitive subject the onset of irritation often follows within an hour or two of the commencement of the

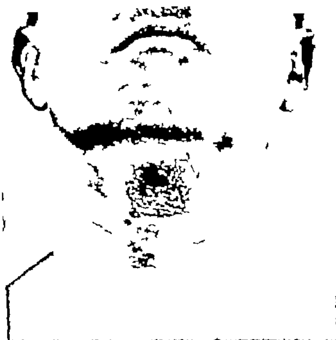


FIG. 16

A localised patch of acute eczema of the front of the neck which followed wearing a necktie of uncreasable material. A patch test with this material was strongly positive. The patient had regularly worn this type of necktie for three years before the skin eruption appeared.

eliciting contact, though it appears sometimes to follow within a few moments. It is seldom delayed more than twelve hours, and in those cases one may suspect that other factors, such as maceration of the skin aiding penetration or the gradual development of sensitivity during the time of contact, are operative. A few experiments I have carried out appear to indicate that the duration of contact required to elicit a positive reaction may be only fifteen minutes. After this, even though the allergen be completely

than in any other (Fig. 15) Weeping is very prone to occur particularly on the scalp and face where the corneous layer is too fragile to allow vesicles to last more than a few hours.

The clinical picture is often very clear-cut, the eruption appearing, at any rate at first, exactly on the site of contact of the allergen with the skin thus greatly facilitating diagnosis (Fig 16) In other cases however the high degree of sensitivity results in a far wider



FIG 15
Acute oedematous facial eczema due to the local application of diphenhydramine. Patch tests to diphenhydramine were positive

involvement of the skin, affecting areas which were never brought into direct contact with the allergen but were contaminated indirectly with the hands The dermatitis due to nail varnish affecting the eyelids neck and possibly the vulva is of this nature and happens to spare the finger nails (Fig 17) this is presumably because the nails are sufficiently thick to provide a barrier to the allergen Most often the eruption affects the areas both of direct and of indirect contact (Fig 18) this is the common sequence of events in many kinds of plant dermatitis where the allergen touches the fingers and hands and is conveyed by them to the face and neck with the result that the eruption appears on all these sites.

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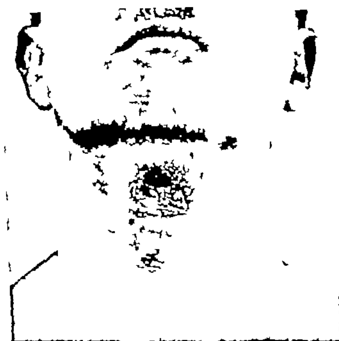


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FIG. 17
A mild degree of redness, oedema and slight scaling of the eyelids. This degree of eczema commonly results from hypersensitivity to nail varnish cosmetics and volatile sensitizers.



FIG 18
Eczematous patches on the sides of the nose w th orb tal oedema and scaling Severe tch ng recurs whenever she wears her spectacles with plastic frames. The eruption ppeared about a week ft r he first obtained these spectacles. Patch test to the material f the plastic frames carried ut on the trunk wer however negat e

removed, the eczematous eruption inevitably develops though its appearance may be delayed for many hours.

The eczema resulting from a single exposure lasting a few hours commonly reaches its height in two or three days. After this it gradually subsides and, in the absence of complications, clears up



FIG. 19

In this woman an eczematous eruption had been intermittently present on the thigh and leg for six years. Suddenly without apparent cause, it became widely disseminated with scaling and crusted lesions, many of them follicular

completely in ten to fourteen days. In those cases where the allergen is not recognised and contact continues the eruption reaches its full intensity also about the third or fourth day and is unlikely after this to make much spontaneous improvement. Instead there is usually a slow extension of the eruption to adjacent parts of the body and the affected area gradually increases in size. In addition to this, an explosive generalised disseminated eczema is liable to appear at any time (Fig. 19) (*see* Chapter IX)

A single episode of contact dermatitis may not clear up so completely after the allergen is removed if the original attack is prolonged. It is often seen for example, that hair-dye dermatitis due to paraphenylendiamine lasts for six or eight weeks, the attack being prolonged presumably because of the difficulty of completely removing the dye. Even after recovery from the dermatitis it is fairly common to see a marked degree of dandruff perhaps with extension to the region of the ears and eyebrows, continue for a year or two afterwards or even longer With this exception it is usually safe to say however that once the allergen is removed there is a very strong tendency to spontaneous recovery and relapses are not likely if the allergen can be avoided

This clear-cut relation of attacks of dermatitis to exposure to the allergen is often of the greatest value in diagnosis. Exposure to allergens may be seasonal or may occur on particular days or after particular activities, so that after two or three attacks have occurred the diagnosis can be established by careful questioning. By attention to the site of origin of the eczema and the time relations of attacks, it is often possible to select a very few substances which are likely to be responsible Patch tests revealing hypersensitivity to one or other of these suspects will then provide valuable evidence.

Patch Tests. In the diagnosis of contact sensitivity it is the patch test which gives the most information It is carried out by applying the suspected allergen to the intact skin in suitable concentration A test patch about one centimetre across should be used and fixed on the skin with adhesive plaster An adhesive must be selected of course to which the patient s skin is not sensitive, and it is an advantage to surround the test patch with a zone of cellophane or similar material so as to isolate the test patch from the adhesive itself For practical use many manufacturers (e g Dalmas) make suitable patches already prepared Substances such as the leaves of plants or wood shavings can be applied direct to the skin cut as thin as possible so as to avoid any pressure effect a drop or two of liquids or powders can be applied to a test patch of plain lint. It is, of course important to avoid primary irritation and to apply the test substance in a concentration which is known to give no reaction in the normal person A list of suitable concentrations for this purpose is given in Appendix A. Patch tests are usually left in place for twenty four or forty-eight hours and the results read immediately on removal and forty-eight hours later

An undoubted positive reaction consists of a vesicular eczematous response (Fig. 20)· any response less than this is doubtful and requires careful interpretation and possibly re-testing with different concentrations of the suspected allergen.



FIG. 20
Positive patch test obtained with Quinolor

Provided patch tests are carried out with substances in suitable concentrations, positive results certainly indicate that the subject is abnormally sensitive to the test substance. It should hardly be necessary to point out, however that this does not necessarily mean that the eczematous eruption under investigation is so caused. At the same time, a negative patch test, although it fails to indicate sensitivity under the particular conditions of testing, cannot be taken as final evidence that an existing eruption is not due to sensitivity to that substance Patch tests do however provide very useful short-cuts in diagnosis and investigation and they may serve the purpose of convincing an incredulous patient of the nature of his disorder

Patch tests should not usually be carried out when the eczema is in an acute phase A positive reaction may at such a time lead to exacerbation of the original eruption and even to widespread dissemination and general systemic upset. Undertaken when the eczema is quiescent and healed, patch tests are unlikely to evoke untoward effects.

The final identification of the cause of contact eczema may ultimately rest on the test of *exposure of the patient to the allergen.* Under carefully controlled conditions the behaviour of the patient's skin is studied when he is ordinarily exposed to the allergen and withdrawn from exposure. Close correspondence between the presence or absence of the eruption and exposure to the allergen ultimately *provides the final proof of the cause of the disease.*

Aetiology and Mechanism. Little is known of predisposing factors to the development of epidermal sensitivity It is clear that damage to or absence of *the corneous layer is likely to facilitate* the development of hypersensitivity to some substances. For example, sulphonamides are unlikely to sensitize intact skin but relatively likely to sensitize skin which has already been damaged by impetigo or eczema Apparently also a factor of personal predisposition *plays some part. It has been shown that people who* have one contact hypersensitivity give a higher number of positive reactions when patch-tested to a battery of routine tests with substances unrelated to their original antigen This was shown by Sulzberger[3] and has been confirmed in my own clinic by Dr Harold Wilson *It is taken to indicate that these subjects are more likely* than the average to acquire epidermal allergic sensitivity On the other hand, epidermal allergy is not clinically linked with other allergic states Whereas asthma hay-fever and urticaria tend strongly to occur in the same individuals, contact sensitivity is entirely separate. Serum antibodies cannot be demonstrated in contact eczema the Prausnitz Küstner reaction is negative, and the only known means of experimental transmission of sensitivity is by the lymphocytes,[4] as detailed in Chapter III

In some of these subjects, though not in all reactions of sensitivity appear on the skin when the allergen is administered by the mouth or parenterally When this takes place the eruption may select areas which were *affected by contact eczema on former* occasions, thus presumably indicating an enhanced sensitivity in those areas.

A man of 35 had corneal ulceration of the right eye for which sulphonamide drops were given. After three weeks he developed contact sensitivity affecting only the right eyelids and immediately adjacent skin Eighteen months later he had tonsillitis and was given sulphonamide by mouth Within twenty-four hours the right eyelids were swollen and weeping an acute eczematous eruption of considerably less severity gradually appeared on the rest of the face and on the hands in the succeeding days.

Areas of former positive patch tests may also flare up after similar provocation. Although in this way some areas of skin, particularly those originally involved in the eruption appear to be more sensitive than the rest of the body surface, this difference in sensitivity cannot often be demonstrated by patch tests. In clinical work it is safe to assume that sensitivity is approximately equal over the whole of the body surface, so that any part of the body can be used for reliable patch-testing.

In many cases group sensitivities occur when the individual will give a positive reaction if brought into contact with substances chemically allied to the original allergen. A familiar example of this sort is with the sulphonamides where a contact sensitivity to one usually implies sensitivity to the whole group.

A sensitivity of this kind once acquired, is probably life-long. There is no doubt that this is true in a *great many* cases. It is, however often said that sensitivity will gradually diminish over the years, but it is doubtful whether such sensitivity is of the type we are now discussing or whether it belongs to one of the categories mentioned below Whether or not sensitivity will spontaneously diminish, there is no doubt that in some circumstances it can be intentionally removed. Epidermal sensitivity to sulphonamides can be abolished by the administration of sulphonamides by mouth. An extremely severe local and general reaction is *liable* to result but desensitization eventually occurs This is certainly not always so with other allergens and successful attempts to desensitize poison ivy reactors have seldom been recorded.

2. CONTACT ECZEMA DUE TO DETERGENTS

(*see also* Chapter VI)

In this class of case damage to the skin by primary irritants plays a vital part.

The First Stage. The initial action of a detergent on the skin is to emulsify and thus remove the fatty constituents of the horny layer then, when the skin is dried, the corneous layer is unable to retain its normal water content and so dries excessively As a result of this the skin becomes slightly scaly it feels rough and loses its normal flexibility Within a short time cracks are liable to form (Fig. 21) This condition is extremely common in housewives and constitutes the first degree of housewives dermatitis. At this stage the changes in the skin are readily reversible and clear up in the



FIG. 1
The tips of the fingers of a dental surgeon whose custom it was to remove instruments from a tray of antiseptic with the tips of the first three fingers. No hypersensitivity was demonstrable and the changes seen are probably all due to the primary irritant effect of the antiseptic.



FIG. —
The left hand of dental mecha ic wh allow d acrylic monomer to run ov the hand many times day Thi liquid i a powerf l fat sol ent. It had damaged the

course of a few days if the patient avoids detergents. Similar damage may be brought about by the continued application of any fat solvent, such as ether (Fig. 22). The degree of dermatitis produced is, however likely to be considerably less since the action



FIG. 23

The right hand of a french-polisher. *He held in this palm a pad soaked in turpentine or white spirit.* The sides of the fingers are also involved. Patch tests were negative.

of alkali common to nearly all cleansers, is not present. Although it is no doubt true that some cleansers are worse in their effects on the skin than others, it seems probable that the qualities required for an efficient cleanser are much the same as those which injure the skin. Thus the search for an efficient non-irritant cleanser is doomed to failure.

In the causation of this grade of dermatitis the exhaustion of the buffer system of the skin surface with loss of neutralizing power of alkali no doubt plays a very important part (Chapter VI). At

this stage of the disease the skin of the affected areas is likely to be sensitive to alkali in the sense only that its neutralizing power is impaired Complete recovery of this power may result if detergents are avoided for a period of some months



FIG. 4
Acute vesicular contact eczema of hands.

The eruptions produced in these cases are ill-defined and are confined to the parts of the body which are directly exposed to the detergent to a considerable degree. In practice they are usually *limited to the hands and forearms* *Their time relations similarly* cannot be sharply delineated The eruption clears up usually within a few days when exposure ceases, but on re-exposure a variable period will elapse before the skin starts to break down again

The Second Stage An important consequence of the first stage of detergent dermatitis is an increase of permeability of the *corneous layer* *As a result of this the detergent more readily gains* access to the subcorneal Malpighian cells, and specific hyper sensitivity may result. To the clinical picture of the first grade of dermatitis there will then be added the features of specific hyper sensitive contact eczema described in the previous section. It is then that vesicles will develop for the first time (Fig 23) weeping also will not usually appear until this stage is reached (Fig. 24) There may also then be a spread of dermatitis to other parts, such as the face which are in very much less contact with the allergen The time relations characteristic of specific hypersensitivity dermat itis are also then likely to be manifested

In these cases specific allergic sensitivity seldom seems however to reach the high degree often seen with the non-irritants

Even when specific sensitivity seems to have resulted, a concentration of 1 per cent. is often necessary in order to elicit a positive reaction in a patch test. The results of patch-testing and the development of recurrent attacks of dermatitis are probably both influenced by the power of the detergent to damage the skin, and to penetrate so as to produce the positive reaction of hypersensitivity. In this way although the degree of true allergic hypersensitivity may not vary over the years the results of patch-testing will, as the corneous layer becomes more or less resistant to the destructive or penetrating power of the allergen.

Other Types of Irritant. Detergents are not the only substances which may lead to this type of dermatitis. A similar sequence of events was observed in connection with acrylic monomer.

This liquid is a powerful fat solvent and gave rise in a dental mechanic to scaling and cracking of the fingers similar to the first degree of dermatitis caused by domestic detergents. Patch tests with monomer were unsuccessful owing to its volatility: patch tests with the polymer were negative. Later on, however, this patient overfilled his petrol lighter with monomer and in this way kept a patch of abdominal skin under his waistcoat pocket wet with the monomer for some hours, a typical vesicular response indicating hypersensitivity appeared on this area.

The common eczematous dermatitis due to cutting oils and soluble oils probably depends on this mechanism. These oils are emulsions of oil and water incorporating surface wetting agents and emulsifiers, and are used as lubricants and coolants in high-speed metal drilling and similar work. They are notorious causes of dermatitis, which they produce probably by the double action of preliminary destruction of the physiochemical integrity of the corneous layer followed by true allergic sensitization.

It seems likely that cement dermatitis is somewhat similar. It has for long been supposed that cement dermatitis was caused entirely by the alkaline action of cement. Pirilä and Kilpiö, however, have recently shown that these patients are all sensitive to chromates; patch tests with cement from which all soluble chromate has been removed by washing, but which is still strongly alkaline, are negative. The actual amount of soluble chromate in cement is, however, extremely small and would probably not be enough to cause a reaction by itself even in a sensitive subject. The probable explanation is that the alkali damages the corneous layer and allows this very dilute solution of chromate to reach the epidermis and excite the reaction. Without alkali, considerably

stronger chromate solutions would be required without chromate, only a minor degree of alkali damage would result.

It will be observed in all these cases, that whatever the degree of allergic sensitivity of the skin the development of an eczematous eruption depends much on the preliminary physiochemical damage inflicted This may explain why allergens must be comparatively concentrated if they are to give positive patch tests

It is unfortunate that dermatitis from detergents occurs so often in housewives who by the nature of their employment find it very difficult to stop work and to avoid exposure to the noxious substance. Rubber gloves worn at this stage are seldom a solution to the problem since the skin becomes worse while they are worn. A change of detergent is sometimes successful but most often it is necessary for the patient to avoid detergents completely for some months. After this rubber gloves may be worn and are likely to afford sufficient protection Dermatitis from domestic detergents seems to have become a good deal more common in the United Kingdom in the last few years, probably owing to the greater efficiency of modern detergents.

The major part of industrial dermatitis is made up of eczematous eruptions of this class *i.e* hypersensitivity of the skin is of a comparatively low order to an allergen which is usually a primary irritant. Whereas, however the eruption in housewives usually remains localized to the hands and forearms eruptions in industrial dermatitis may spread much more widely and run a very much more protracted course The reasons for this will be considered below

Non-Specific Intolerance of Treatment. It may be appropriate here to mention the peculiar variable intolerance of treatment often seen in eczema It is commonplace that in the more active stages of eczema particularly in the weeping stage, the eruption may be greatly aggravated by treatment which is well tolerated elsewhere on the skin and, indeed, on the self-same areas later on, when the eczematous process is less active It is said that the physical nature of the application is important, since impervious greas tends to warm the skin surface and watery lotions or creams to cool it I have been unable to confirm these observations. At the same time it can hardly be doubted that a very important factor is the presence and thickness of the corneous layer and its state of physiochemical integrity as affected by the eczematous process To this is added a

possible mildly irritant action on the Malpighian cells, perhaps with some degree of true allergic sensitivity (*See also* Chapter III on status eczematicus.")

3. CONTACT ECZEMA PROVOKED BY FRICTION

A third type of contact eczema is that in which sensitivity to nickel plays a part. In most cases the patient is a woman and the eruption starts under the buckle of a new stocking-suspender Patch tests to nickel sulphate are positive and the condition clears up when the suspender buckles are removed.

In many cases of a similar sort, however the sequence of events is not so simple. Very often it is observed that the eruption occurs under some suspender buckles but not all, it is not unusual for secondary disseminated eczematous patches to appear on other parts of the body particularly on the antecubital regions and sides of the neck. In a few cases it has seemed to be clearly established that the " secondary patches appeared a few weeks before the primary ones; furthermore, in some patients an eruption starting as suspender-buckle dermatitis spreads to other parts of the body and continues for an indefinite period even though all contact with metal articles had ceased. When the eruption persists indefinitely in this way it may often clear away from the primary areas and remain only on the secondary ones.

Vesicles are not usually seen in this type of eczema. The skin is very red, with a slightly swollen succulent appearance, and scratching leads to weeping excoriations (Fig. 25) Lichenification is common. It seems certain that the secondary eruption in these cases is of different nature and arises by a different mechanism from the disseminated eczema which follows contact eczema due to specific allergic sensitivity The patient scratches a great deal and it seems that friction is the chief mechanism by which the eruption is perpetuated.

Nickel Sensitivity It is strange how seldom contact dermatitis seems to arise on the hands from handling nickel articles Nickel dermatitis nearly always seems to require prolonged contact of metal with the skin with the addition of friction or pressure. It is seldom if ever seen on the thighs of thin women in whom the suspender buckles fit more loosely

The results of patch tests in these cases are very variable; often the skin reacts to nickel sulphate solution in a dilution of 3 or 5 per cent. but no weaker In other cases very high dilutions

produce a positive result In many cases patch tests carried out with a small metal article are positive; here the actual concentration of metal available in soluble form must be extremely small In a great many of these cases the impression is strongly gained that



FIG. 5
Suspender buckle dermatitis present for eighteen months in a woman aged 51 Six months later the side of the neck was affected The eruption on the thighs gradually cleared up when the suspender buckle was removed but the eruption on the neck remained in this situation it was subject to periodical exacerbations and remissions which followed anxiety over her husband's health.

the patient's temperament, possibly with emotional tension is responsible for itching and scratching and the perpetuation of the disease, and that sensitivity plays a subsidiary part arising only after the eruption has developed

When nickel sensitivity can be demonstrated it may tend to preoccupy the mind of the doctor and perhaps of the patient too When it is not present and the eruption appears more diffusely on the antecubital areas neck and inner aspect of the thighs its relation to emotional upsets and tensions becomes very striking

INDUSTRIAL DERMATITIS

The large proportion of cases of industrial dermatitis are eczematous in nature. Those conforming to the first group and

associated with a high degree of specific hypersensitivity are usually recognised without difficulty and present no insuperable problem provided the patient can avoid exposure to the allergen in future. A considerably greater proportion of patients belong to the second group where eczematous dermatitis is due to contact with primary irritants of detergent or fat-solvent type to which the patient's resistance is moderately reduced. It is for this reason that industrial dermatitis is very often due to cleaning the skin after work with turpentine, thinners or strong alkalis rather than to contacts which occur during the actual work. These cases do not usually give rise to great difficulty in diagnosis. A change of occupation is not always necessary provided the patient will take greater care in handling irritants. It is well known that in some kinds of industrial dermatitis the eruption will gradually clear up although the patient remains at work. This process, known as "hardening," probably occurs most often with cases in this type of dermatitis due to primary irritants.

A third type of industrial dermatitis appears to resemble the suspender-buckle group in many ways. It commonly appears for the first time on the hands and forearms, sometimes on the neck or on the legs. The eruption is intensely itchy and may take the form of an acute vesicular or weeping eczema but more often develops as excoriated papules followed by lichenification. In this class of case the exact diagnosis and the relation of the disorder to work presents a most difficult problem. The site of origin of the eruption seems to indicate that work is playing a part; sometimes the workman is handling primary irritants but often the work is of a dusty or dirty nature but without exposure to identifiable allergens or primary irritants. The work may indeed involve handling no suspicious substance and the eruption be attributable to fumes or similar vague influences.

The time relations may also be confusing. It is common for the eruption to become worse after work is stopped and thereafter to run a protracted course in which exacerbations and remissions do not correspond to changes in work contacts. The disorder may become very widespread but is usually limited to the limbs and head.

It is rather common in dirty dusty occupations for an eruption to begin around or immediately above the ankles. This is one of

British workmen often regard industrial dermatitis as an infection due to germs caught at work or to dirty conditions and attach little significance to the chemical nature of the things they handle.

the common sites to be affected in coalminers In these cases coal dust can usually be seen filling the follicles, which are raised into reddened excoriated papules no true sensitivity to coal can be demonstrated and it seems that the dust is providing a mechanical stimulus sufficient to start off itching and excoriation which are then perpetuated in a susceptible subject by psychic tension

An important feature in these cases is that the patients are extremely often unhappy worrying people, often involved in litigation over the compensation they are receiving or think they should receive for industrial disease, and the impression is strongly gained that a good deal of their trouble is psychogenic. On the other hand it is equally clear that most of these patients suffer financially a great deal from their disease and their affliction can bring them very little conscious satisfaction Even if it is accepted, however that the perpetuation of this dermatitis is chiefly due to scratching because of an itch which is psychogenically caused it may be that in many cases exposure to an industrial irritant started off the symptoms and was thus the immediate cause of the dermatitis; had this cause never been applied the entire skin disorder psychogenic or otherwise, would not have occurred or at least would not have taken the form of dermatitis.

This assessment of the relative importance of various factors in any individual case is a very difficult matter and allows for every shade of opinion. Different experts will usually agree that the various factors are present, but may diverge considerably in their views as to which are the most important. Legal difficulty arises when compensation for industrial disease is to be paid and responsibility for the disease allocated Generally speaking the law takes the view that when a multiplicity of causes are present the "cause" of the eczema is the immediate precipitating factor and not the predisposing or underlying causes, however prominent a part they may play in contributing to the onset of the disorder Although therefore, the development and perpetuation of an eruption may be largely due to psychic abnormality the skin disease would be regarded as industrial in origin if it were thought that it was precipitated by contact with an industrial irritant and that it would probably not have occurred if the person had not been in contact with irritants These cases gain in difficulty because they are liable to last a very long time, and to give rise to much unhappiness and loss of wages It has repeatedly been noticed that after complete

resistance to treatment they may clear up quickly when financial compensation is settled to the patient's satisfaction.

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CHAPTER III

ALLERGIC ECZEMA THEORETICAL CONSIDERATIONS*

H HAXTHAUSEN

DEFINITION

THE term "allergic eczema" means a skin affection presenting all the clinical and histological characteristics of eczema produced on exposure to the action of a certain substance to which the skin has become sensitized beforehand The sensitization as a rule, takes place on a single or repeated exposure of the skin to the substance concerned and an allergic reaction is elicited—also as a rule—on subsequent exogenous action of the substance upon the skin. This is due, however to the circumstance that in either case it is the *epicutaneous* action of the substance which most frequently takes place in practice But it has been established that the sensitizing as well as the eliciting exposure can occur for instance with subcutaneous or intramuscular injection

A great number—nay probably a majority—of the substances able to produce allergic eczema are fairly simple chemical compounds many of which at any rate in higher concentrations, have a direct toxic effect on the skin Even though such a toxic effect *sometimes may develop with features resembling those of eczema* —as for instance, croton oil eczema—there is still a decisive difference between this primarily toxic reaction and the allergic In the first place, the latter is most often induced by concentrations much lower than the toxic and affecting only sensitized individuals *Secondly the features of the two reactions are essentially different*, as is evident especially on histological examination In particular

* The term allergic eczema is to be taken meaning allergic eczematous dermatitis throughout this chapter; in Chapter IV allergic eczema is given as one of the synonyms of atopic dermatitis, but is not to be interpreted in this way in this chapter *Ed.*

the cells characteristic of inflammatory processes show this difference: the toxic reaction is accompanied by an exudate containing mainly granulocytes, whereas the allergic eczematous reaction is characterized chiefly by mononuclear cells, especially lymphocytes (Nexmand, Baer and Yanowitz[1]) Thus the allergic eczema reaction cannot be interpreted as an accentuated toxic reaction, but it has its own characteristic picture and, furthermore, it may also be produced by substances having no direct toxic effect on the skin.

PATHOGENESIS

Our knowledge of the pathogenesis of allergic eczema is derived chiefly from animal experiments, for which in particular guinea pigs have been employed. In contrast to the state of hypersensitiveness due to true so-called complete antigens, and which can be produced in many different animals with more or less ease, eczematous hypersensitiveness is limited to relatively few species It has been possible to produce this form of hypersensitiveness with certainty only in man, guinea-pig, monkey ferret, pig and chicken, whereas, for instance, rabbits which are very suitable for the production of "true" antibodies, cannot be sensitized with substances producing eczema in the aforementioned species (Rostenberg and Haeberlin) Guinea-pigs can be sensitized with many different substances, among which 2 4 dinitrochlorbenzene is probably the one most commonly used, giving almost constant positive results. Race, food and individual characters, however play a not inconsiderable rôle with regard to the capacity of the animals for sensitization Animals that are markedly sensitized by one substance may very well be sensitized but slightly by another while other animals of the same race may be sensitized strongly by the latter substance and only slightly by the former It would not therefore be generally correct to say that the capacity for sensitization of a given animal is great or slight.

When a limited area of the skin of a guinea-pig is painted with a 5 per cent. solution of 2 4 dinitrochlorbenzene, slight redness of this area will appear within twenty-four hours and then subside during the following day When the sensitiveness of the skin is now tested from time to time, for instance by painting a small fresh area with a 1 per cent. alcoholic solution of the substance, this treatment will not produce any reaction, or at most, a slight erythema. Not until a certain latent period has passed—as a rule, about twelve days—does this test application produce a

characteristic reaction, red *papular infiltration of the skin*. This phenomenon cannot be called a true eczematous reaction and hence it has been criticized as a false analogue of allergic eczema. In man, however sensitization with dinitrochlorbenzene can be performed almost as easily as in the guinea-pig and in man the elicited allergic reaction meets all the requirements reasonably made of an eczema It is very likely that the different picture presented by the *guinea-pig is merely due to the circumstance that in this animal no* vesiculation takes place on account of particular anatomical or physiological conditions in the skin Once hypersensitiveness is produced it persists for a very long time, both in guinea-pig and man It may vary somewhat in intensity but on the whole it shows a tendency to subside partly or completely within some months (guinea pig) or years (man) The hypersensitiveness is specific, *i.e.*, it is directed exclusively against the particular substance employed for the sensitization—though with this exception that very closely related chemical compounds are also able to produce a reaction which as a rule is noticeably weaker than the one produced with the original substance.

This sensitization can be prevented or attenuated in various ways as, for instance, by administration of the antigen in suitable doses during the period of sensitization (Sulzberger Chase) a fact for which no plausible explanation has so far been advanced. Hollström found that sensitization of man with dinitrochlorbenzene failed in most cases if the subject was given pyretotherapy (malaria) at the same time. Under these conditions a slight degree of hyper sensitiveness *was produced only in two out of fifteen subjects*, while strong hypersensitivity appeared in thirteen out of fifteen controls.

The specificity as well as the characteristic latent period reminds one strikingly of the features encountered in true anaphylaxis and other antigen-antibody reactions and at first indeed attempts were made to explain the eczematous sensitization as a phenomenon related thereto One of the earlier and more weighty objections *to this hypothesis* was the fact that eczematous allergy is most often produced by relatively simple chemical compounds—substances *which on ordinary parenteral injection have no antigenic* effect This objection has been ruled out—at any rate in part—by Landsteiner who demonstrated that many substances in this category acquire antigenic properties on artificial linkage with proteins and on injection induce the formation of antibodies to the simple compound concerned Now it is unlikely that such formation

of antibodies gives rise to the eczematous hypersensitiveness; for if this be due to antibodies, they must be of a nature different from that of the usual ones. Nevertheless, Landsteiner's experiments have shown the possibility of antigenic effect even in using simple chemical compounds.

Among the substances producing allergic eczema a very great number are able to combine with proteins. This applies, for instance to salts of mercury and chromium, and also to 2 4 dinitrochlorbenzene, which has been employed extensively in animal experiments, and in which the very labile Cl atom is readily replaced by radicles of protein molecules. It also applies to a substance such as paraphenylenediamin, which as shown by Mayer is oxidized in the skin to amidoquinones that react with NH and SH groups in protein. In numerous other substances, however we know of no particular affinity for protein, but it is quite possible that enzymatic and other processes in the skin may in such cases play a rôle in the linkage to protein.

If such a linkage is to take place, the "simple" substance will probably have to act on protein at a suitably high concentration and for a suitably long time. These conditions are met especially in the usual process of sensitization with direct application of a fairly concentrated solution to the skin. Miescher[2] has strikingly demonstrated the significance of the concentration when he painted guinea-pigs with a 0 25 per cent. or 0 05 per cent. alcoholic solution of dinitrochlorbenzene. The stronger solution produced hyper sensitiveness even when only small skin areas were painted with it, whereas the weaker solution was inactive even when applied to such large areas that the total amount of the substance employed was considerably greater than in the positive experiments.

In order to act as an eczematous antigen, the substance employed does not necessarily have to be linked only to proteins of the skin. It has also proved practicable to produce eczematous hypersensitiveness by parenteral injection of substances already linked to other proteins—e.g., serum of the experimental subject. Thus, intramuscular injection of ten ml. serum to which dinitrochlorbenzene has been added to a concentration of 0 05 per cent. on the preceding day not infrequently produces hypersensitiveness in man, whereas the same amount of the substance in saline is found to be inactive (Haxthausen[*]). Even though this substance presumably is not linked completely with the serum proteins, these

characteristic reaction red papular infiltration of the skin. This phenomenon cannot be called a true eczematous reaction and hence it has been criticized as a false analogue of allergic eczema In man however sensitization with dinitrochlorbenzene can be performed almost as easily as in the guinea pig, and in man the elicited allergic reaction meets all the requirements reasonably made of an eczema It is very likely that the different picture presented by the guinea pig is merely due to the circumstance that in this animal no vesiculation takes place on account of particular anatomical or physiological conditions in the skin Once hypersensitiveness is produced it persists for a very long time, both in guinea-pig and man It may vary somewhat in intensity but on the whole it shows a tendency to subside partly or completely within some months (guinea pig) or years (man) The hypersensitiveness is specific *i.e* it is directed exclusively against the particular substance employed for the sensitization—though with this exception that very closely related chemical compounds are also able to produce a reaction which, as a rule is noticeably weaker than the one produced with the original substance.

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The specificity *as well as the characteristic latent period reminds* one strikingly of the features encountered in true anaphylaxis and other antigen-antibody reactions, and at first, indeed attempts were made to explain the eczematous sensitization as a phenomenon related thereto One of the earlier and more weighty objections to this hypothesis was the fact that eczematous allergy is most often produced by relatively simple chemical compounds—substances which on ordinary parenteral injection have no antigenic effect. This objection has been ruled out—at any rate in part—by Landsteiner who demonstrated *that* many substances in this category acquire antigenic properties on artificial linkage with proteins and on *injection induce the formation of antibodies to the* simple compound concerned Now it is unlikely that such formation

of antibodies gives rise to the eczematous hypersensitiveness; for if this be due to antibodies, they must be of a nature different from that of the usual ones. Nevertheless, Landsteiner's experiments have shown the possibility of antigenic effect even in using simple chemical compounds.

Among the substances producing allergic eczema, a very great number are able to combine with proteins. This applies, for instance, to salts of mercury and chromium, and also to 2 4 dinitrochlorbenzene, which has been employed extensively in animal experiments, and in which the very labile Cl atom is readily replaced by radicles of protein molecules. It also applies to a substance such as paraphenylenediamin, which, as shown by Mayer is oxidized in the skin to amidoquinones that react with NH and SH groups in protein. In numerous other substances, however we know of no particular affinity for protein, but it is quite possible that enzymatic and other processes in the skin may in such cases play a rôle in the linkage to protein.

If such a linkage is to take place, the "simple" substance will probably have to act on protein at a suitably high concentration and for a suitably long time. These conditions are met especially in the usual process of sensitization with direct application of a fairly concentrated solution to the skin. Miescher* has strikingly demonstrated the significance of the concentration when he painted guinea-pigs with a 0 25 per cent. or 0 05 per cent. alcoholic solution of dinitrochlorbenzene. The stronger solution produced hyper sensitiveness even when only small skin areas were painted with it, whereas the weaker solution was inactive even when applied to such large areas that the total amount of the substance employed was considerably greater than in the positive experiments.

In order to act as an eczematous antigen, the substance employed does not necessarily have to be linked only to proteins of the skin. It has also proved practicable to produce eczematous hypersensitiveness by parenteral injection of substances already linked to other proteins—*e.g.*, serum of the experimental subject. Thus, intramuscular injection of ten ml serum to which dinitrochlorbenzene has been added to a concentration of 0 05 per cent. on the preceding day not infrequently produces hypersensitiveness in man, whereas the same amount of the substance in saline is found to be inactive (Haxthausen *). Even though this substance presumably is not linked completely with the serum proteins, these

experiments show indisputably that it must be the linkage products, not the free substance, that are active.

In practice however the chance of linkage will be greater on application to the skin or on intracutaneous injection Intravenous or intramuscular injection of the pure substance does not lead to sensitization—presumably because it is diluted and absorbed too rapidly for any linkage to take place. *In contrast to this, sensitization* may be obtained by injecting the substance into lymph nodes, as shown by Seeberg [1]—an observation of particular interest because the lymphocytes presumably play an important rôle in antibody formation

Assuming now that linkage to protein is the first stage in the process of eczematous sensitization the next question will be whether the antigen formed in this way exerts its effect locally in the skin or only after absorption or possibly whether both modes of action take place simultaneously The fact that successful sensitization as a rule is universal—*i e.,* comprising the entire skin surface—makes an absorptive effect rather probable. Landsteiner and Chase have shown that guinea-pigs failed to become sensitized to poison ivy extract when the painted skin area was excised within eight to twelve hours, whereas later excision did not prevent the sensitization. These investigators further showed that when deep incisions were made round a painted area of the skin, sensitization *failed in the isolated skin area as well as outside. If on the other* hand, the skin outside the " island " was painted primarily hypersensitiveness developed in the " island " as well as outside. With more superficial incisions, hypersensitiveness developed in the " island " as well as outside, no matter whether the " island " or the *surrounding skin* was painted primarily Presumably the outcome of these experiments has to be interpreted as follows the hypersensitiveness is due *to absorption of an antigen formed in the* skin by linkage of the specific substance to protein This absorption appears to take place by way of the lymphatics (which are divided by the deeper incisions and not by the superficial) This is quite in harmony with the assumed protein nature of the antigen After the absorption an " antibody " or kindred factor is formed and this is later carried to the skin by means of the blood stream

The above *experiments speak decidedly in favour of eczematous* sensitization not being limited locally to the skin but brought about by internal factors *that are activated after absorption of the antigen.* However other experiments have been reported that are highly

suggestive of local sensitization. Thus, Strauss and Coca found that when monkeys were sensitized with poison ivy extract applied to the forearm, and a circular incision was then made proximally to the painted area hypersensitiveness developed—but only in skin areas peripheral to the incision. Conversely painting of the skin proximal to the incision produced no hypersensitiveness of the isolated skin of the arm, whereas all the entire remaining skin surface became hypersensitive. Similar results have been obtained in guinea-pigs by Schreiber and Müller

Various clinical observations have also been taken as supporting the theory of the occurrence of local eczematous sensitization. Thus it is well known that in some cases of localized allergic eczema positive patch tests are obtained only when the patches are placed in the vicinity of the skin area attacked. As a matter of fact, however the skin just outside a fresh eczematous eruption is undoubtedly in a more "labile state than the skin elsewhere, *i.e.*, the skin here reacts more readily and more strongly to non-specific irritants too So the apparently local hypersensitiveness might conceivably be due to such a non-specifically increased capacity to react.

In the experimental sensitization of man with dinitrochlorbenzene, applied to quite small skin areas, the hypersensitiveness is sometimes seen—at any rate apparently—to be limited to the areas painted originally But here too the question arises whether this phenomenon be not attributable to non-specific factors (an increased lability of the skin in these areas) as universal sensitization—if sufficiently weak—will also manifest itself only within these labile skin areas.

Haxthausen has tried to solve the question by applying dinitrochlorbenzene to a quite minimal skin area. His procedure consisted in introducing a needle dipped in the melted substance, through the epidermis. If purely local sensitization be at all possible it could be expected to develop in this case, as the size of the area exposed cannot be relevant if only the concentration of the substance applied is sufficiently high On the other hand, it is obvious that the total amount of antigen formed must determine whether a universal sensitization appears. Furthermore, with the experimental technique here employed only a minimal amount of antigen can be absorbed. Now the experiments showed that within the first twenty-four hours after the prick a tiny red, infiltrated papule appeared, and disappeared again within a few days. But in subsequent tests no

hypersensitiveness could be demonstrated—neither at the site of the prick nor anywhere else on the skin

On treatment of a slightly larger skin area—*e.g* punctate application of thirty per cent dinitrochlorbenzene by means of a small cotton swab—an apparently localized hypersensitiveness is often observed and also frequently universal hypersensitiveness, here the rest of the skin however gives a noticeably weaker reaction than the primarily painted area

That local sensitization still *may* occur is evident from Edmund s[44] *experiments with injection of dinitrochlorbenzene into* the cornea of guinea-pigs A minimal amount, 0 02 ml of a 0 05 per cent solution in saline + 5 per cent. alcohol injected into one eye produced local hypersensitiveness manifesting itself by the fact that reinjection two weeks later gave rise to characteristic keratitis, whereas the other eye (injected beforehand with saline + 5 per cent. alcohol) developed no keratitis on injection of dinitrochlorbenzene The keratitis could not be elicited by intraperitoneal injection of the substance and animals sensitized in the usual way by painting of the skin did not get keratitis on subsequent intracorneal injection The animals sensitized in the cornea showed a negative reaction to painting of the skin with the substance. It appears therefore as if the cornea may become the site of real local sensitization—*something which presumably is due to the circulatory* isolation of this organ from the rest of the body

ANTIBODIES IN ALLERGIC ECZEMA

For some time past attempts have been made in many different ways to demonstrate the presence of antibodies in allergic eczema All direct serological methods have constantly given negative results and the few positive results obtained in experiments on passive sensitization with the Prausnitz Küstner technique have not been able to stand more thorough examination Probably the explanation of the positive results reported with this method is that *eczematous allergy is not infrequently combined with* urticarial allergy and presumably it is urticarial allergy that has been transmitted

Some additional positive results have been obtained with the *Urbach Königstein method which differs from the abovementioned* in that the content of cantharides blisters, not blood serum is used for intracutaneous *injection after which patch tests or intracutaneous* tests are performed with the antigen. The reaction is read

after twenty-four hours, while in the Prausnitz-Küstner test it is read after fifteen to thirty minutes. Urbach has reported a good many cases in which passive transmission of hypersensitiveness is said to have been successful; and even though their number is small as compared to the numerous negative results, they might be taken to indicate that such transmission now and then really takes place Possibly the cell content of the vesicular fluid is here the decisive factor (*see below*) Curtis[1] attempted passive transmission with extracts of allergic skin (obtained by trituration of such skin) but the results were altogether negative.

In contrast to several true antibodies, the hypothetical " eczema antibody does not pass through the placenta, for the offspring of sensitized guinea-pigs constantly shows a negative reaction In agreement with these findings, experiments have been recorded by Grolnick[1] who sensitized pregnant women with an alcohol extract of the plant Krameria In no instance could hypersensitiveness be demonstrated in the children of these women. These observations are quite in harmony with the " lymphocytic hypothesis " that will be mentioned later on.

A considerable advance in this field of research was made when Landsteiner and Chase discovered that hypersensitiveness *to picryl chloride*—which has to be considered analogous to eczematous allergy—can be transmitted with the cells from artificially produced peritoneal exudate from sensitized guinea-pigs to normal animals when a sufficient amount of the cellular suspension is injected intracardially or intraperitoneally As by far the preponderant part of these cells is made up of lymphocytes, it seemed obvious to take them to be carriers of the effect. Indeed, transmission of the sensitization was found practicable also with suspensions of thymus cells, containing almost exclusively lymphocytes, in experiments on guinea-pigs sensitized with dinitrochlorbenzene (Haxthausen ') Furthermore transmission of hypersensitiveness has proved practicable also with the white blood cells. As other experiments, moreover have shown that the granulocytes ar inactive in this respect, the experiments with white blood cells also indicate that the *lymphocytes are carriers of the effect* (Haxthausen) This effect is associated with the living lymphocytes, as it is abolished even by such gentle treatment as freezing, which would hardly destroy a preformed antibody

The way in which the effect is transmitted to the cells of the skin is as yet completely obscure So far all experiments on *local*

passive sensitization—with intracutaneous injection of lymphocyte suspension and following application of the antigen—have turned out negative Haxthausen[17] attempted local transmission with white cells from sedimented blood and lymphocytes from excised lymph *nodes of patients with allergic eczema* but obtained no definite positive reaction. Later Baer and Sulzberger[18] and Baer Serri and Kirman[19] attempted transmission with sedimented white blood cells, employing a technique which had been used successfully by Lawrence for transmission of tuberculin allergy (sedimentation of the red cells in heparinized blood with bovine fibrinogen centrifuging of the plasma fraction) The results were negative, however and this also applies to the results obtained by Haxthausen [1] with a *similar experimental technique, merely with employment of dextran instead of bovine fibrinogen*

So far then local passive transmission of eczematous allergy has not been practicable whereas such transmission of tuberculin allergy has been carried out successfully by several investigators on animals as well as man (Metaxas and Metaxas-Bühler[21], Lawrence, Wesslén[3]) Although the two forms of allergy are alike in many respects they thus seem to differ on this particular point. But *perhaps this difference is merely apparent, and it may conceivably* be due to the particular difficulties associated with the demonstration of eczematous allergy

So we only know with certainty that in guinea-pigs the eczematous allergy can be transmitted with lymphocytes when these are injected in a sufficient amount and in such a way that they are absorbed and find their way to the skin through the blood stream. As yet we do not know whether the lymphocytes themselves form the active principle or whether they merely act as " carriers " of this principle; nor do we know how it is given off to the skin So far it has not been possible to extract the active principle from the *cells nor demonstrate any secretion of it by the living cells. No* doubt a particular mechanism is involved here as the lymphocytes give off no active substance to the blood plasma with which they are in intimate and protracted contact. Injection of even large amounts of plasma from sensitized guinea pigs into normal ones does not bring about any passive sensitization (Haxthausen) As a matter of fact, the active principle appears to be attached very loosely to the cells of the skin if there be any such linkage at all (see the section " *Transplantation Experiments* ")

Whether the lymphocytes produce or merely transport the hypothetical antibody—nay even if the active principle be of an entirely different nature—it is plainly evident from animal experiments that this principle is dependent on vital processes in the lymphocytes. As soon as the lymphocytes are killed, in one way or another this effect is lost. So it would seem reasonable to expect that procedures destroying or damaging the lymphocytes of the organism would also bring about a reduction of the eczematous allergy. But on universal X-radiation of guinea-pigs sensitized with paraphenylenediamine, Cohen, Mayer and Criep[1] could demonstrate only a moderate decrease in the epicutaneous reaction, while the intracutaneous appeared not to be affected by the treatment. On local X-radiation of the skin of sensitized guinea-pigs Haxthausen[73] found no distinct weakening of the eczematous reaction even after employment of large doses (10,000 r Bucky rays). In experiments with radium emanation placed in celluloid capsules on the skin for twenty-four hours—which affect also the lymphocytes emigrating during the development of the eczema reaction—a decrease in the reaction was found only when the radiation was strong enough to produce a somewhat necrotic tissue reaction. The result was the same whether the test was performed immediately before the emanation and the reaction was read on the following day or whether the test was performed after twenty-four hours emanation and the reaction read on the following day.

Thus the universal as well as the local damage to the lymphocytes that may be produced by the radiation have afforded no positive proof of the rôle these cells are assumed to play nor of course, any proof against this assumption.

The rôle of the lymphocytes in the pathogenesis of allergic eczema thus still includes many unsolved problems. That these cells may transmit the active principle to cells of the skin is evident from the observation made by Kondo[1-] that normally a fair number of lymphocytes are present in the skin, not only in the corium but also in the epidermis even as far up as the stratum spinosum. This finding, confirmed by later investigators (e.g. Andreasen[17]) shows indeed that a not inconsiderable migration of lymphocytes from the blood stream into the skin also takes place normally. Lymphocytes play a conspicuous rôle too in the development of the eczematous-allergic reaction, as the immigration of these cells is one of the very earliest signs which can be demonstrated not infrequently even before the characteristic changes in the epidermal cells become

visible (Miescher[11]) It should also be reiterated that the cell content of allergic eczema vesicles consists mainly of lymphocytes (e g Nexmand [1 1] Miescher[11])—*in contrast to blisters from toxic agents* where granulocytes predominate

TRANSPLANTATION EXPERIMENTS

It has proved practicable to elucidate some important findings concerning the pathogenesis of allergic eczema by *transplantation* experiments In these experiments the principle has been to transplant *skin from an eczema-allergic person to a normal one and* conversely normal skin to an eczema-allergic subject Thus it *becomes possible to investigate whether the allergy is associated* with the epidermal cells or is due to factors transmitted from th allergic host.

The first experiments in this field were probably carried out by Bruno Bloch who transplanted a Thiersch graft from a pati nt suffering from iodoform eczema and a corresponding graft from a normal subject onto a patient with a granulating burn The next application of iodoform produced redness and vesiculation of the iodoform graft " while the normal graft gave no reaction Th transplant soon became detached however Similar experiments have been performed by Klausner Bircher and Tzanck Bensaude, Cachin and Dobkevitch —all *with negative results*

The outcome of these older transplantation experiments can b evaluated only with reservations as it was not then fully realized that homotransplants do not heal permanently but become detached after a while Permanent healing can be obtained only on trans plantation between uniovular twins as done by Haxthausen in th following way one twin was sensitized by painting a skin area (about 5 by 5 cm) once with a 30 per cent solution of dinitrochlorbenzene in acetone The appearance of hypersensitiveness was ascertained by painting another area with a 1 per cent. alcoholi solution which now produced an eczematous reaction Then a Thiersch graft was transplanted from the allergic skin to the untreated twin and *vice versa* by simple exchange of the two grafts. Then after complete healing of the grafts a new test was made by painting the graft and some of the surrounding skin with a 1 per cent. solution The result was the same in two pairs of twins examined namely after transplantation to a non-allergic host the sensitized skin loses its capacity for reaction and conversely after

the normal skin graft has healed in the allergi host it acquires this property

Later these experiments were expanded as it was found that homotransplants—at any rate, in several cases—could heal temporarily and become vascularized sufficiently long for th establishment of an eczematous reactivity even though the grafts always became detached later on In these complementary experiments Haxthausen found similar conditions as in the twin experiments. In fourteen successful transplantations of normal skin to eczema allergics the patch test thus produced a positive reaction in the transplant as well as outside it in eleven cases. In converse experiments—allergic skin transplanted to a normal host—in seventeen successful transplantations a positive patch test on the graft was found only in two cases—and even these two reactions were not quite convincing.

The conclusions that may be drawn from the transplantation experiments are: *that the allergy must be due to a factor supplied to the skin from within*, whether it be an antibody supplied by way of the blood stream or some other mechanism. In so far as th active principle becomes attached to the epidermal cells, this linkage must be very loose as the principle disappears within a few days. It follows that eczematous allergy can hardly be such a constant and persistent state as is usually imagined—for often eczematous allergy remains apparently unchanged through many years—but rather a state in which the active principle is supplied to the skin steadily while at the same time it is subject to destruction too In other words, it is rather a question of a state of equilibrium than of a fixed alteration.

The experiments show quite plainly that eczematous allergy cannot be due to any particular acquired property of the epidermal cells. At any rate, such hypothetical changes alon cannot explain the reactions observed.

It cannot altogether be excluded that the principle which is conveyed from the allergic host to a transplanted normal graft and renders this hypersensitive might originate from the underlying connective tissue But experiments performed on guinea-pigs speak decisively in favour of an active principle being transmitted to the skin by way of the blood stream. Haxthausen[13] sensitized guinea-pigs with dinitrochlorbenzene and then united the sensitized animals with normal partners by means of abdominal parabiosis. It could

be demonstrated in this way that the untreated partners within a few days became passively sensitized.

Taking everything into consideration it appears that eczematous allergy depends upon an agent supplied to the skin by way of the blood stream—whether it be an antibody or some other factor As will be noticed the outcome of the transplantation and parabiosis experiments is quite in harmony with the theory that has been gaining ground rapidly in recent years namely *that the lymphocytes in the blood not dissolved antibodies transmit the capacity for reaction to the skin*

According to clinical and histological observations the eczematous reaction is strongly indicative of damage to the epidermal cells and possibly also other cells in the skin. *A priori* it seemed natural to regard this damage in a similar way to for instance, haemolysis by some specific antigen So far however experimental research has been unable to reveal any such damage In transplantation experiments with so-called pinch grafts"—quite small superficial skin pieces of about 2 × 4 mm —transferred to granulating wound surfaces Haxthausen observed the following features. pinch grafts *taken from allergic skin that had been exposed to the action of the* specific antigen beforehand by electrophoresis or in some other way *showed the same intensity of growth as did untreated grafts.* Untreated " pinch grafts " from allergics grew like normal growths and showed no distinct inhibition of growth when after "*taking*" they were exposed to the action of the specific antigen In an allergic receptor autotransplants after exposure to the specific antigen showed no arrest of growth as compared to homotransplants.

These results especially the last-mentioned, showed that exposure to the specific agent does not noticeably reduce the vitality of the epidermal cells and this might indicate that the not inconsiderable changes characteristic of the allergic eczema reaction are hardly primary but rather result from exudation oedema formation in the cells etc —*i e* changes in a primarily normal skin structure Nor has it been possible indeed in the " pinch graft " experiments to demonstrate true eczematous changes This, however may not be due exclusively to entirely anatomical features but also to the possible circumstance that newly formed, growing epidermis may differ immunologically from ordinary epidermis In this connection it is to be emphasized that the tiny " pinch grafts " here employed behave identically as regards intensity of growth no matter whether they are autotransplants or homotransplants.

Furthermore, homotransplants usually last much longer than Thiersch grafts—and apparently permanent healing is, at all events, by no means infrequent.

Attempts have also been made by means of tissue cultures to elucidate the question of the assumed noxious effect of the antigen on the epidermal cells. Everett, Livingood, Pomerat and Hu[17] grew epidermis from patients with allergic eczema and then exposed th cultures to the action of the specific antigen. They were unable in this way to demonstrate any higher sensitiveness to the specific antigen in these, as the "minimal inhibitory dose" and the "least injurious dose" were about the same here as in control experiments with normal skin—a result that is quite in harmony with the transplantation experiments. These tissue culture experiments, however do not allow of far-reaching conclusions, as, among other factors, the rôle assigned to the lymphocytes in eczematous allergy cannot be manifested here.

SITE OF THE ECZEMATOUS-ALLERGIC REACTION

The allergic eczema reaction is generally assumed to be elicited *through* a specific stimulation of the epidermal cells, accompanied by various secondary phenomena which also involve the corium. Presumably this assumption is based primarily on the histological findings which indisputably present the most conspicuous and characteristic changes in the epidermis. It is obvious, however that this circumstance in itself is no proof of the primary rôle that has been assigned to the epidermal cells; and the same applies to the investigations carried out in order to see which changes first become visible For indeed, it is quite conceivable that changes of decisive pathogenetic significance cannot be recognised simply by examination of stained sections.

On this account the many subtle histological studies carried out to elucidate the pathogenesis of allergic eczema will not be reviewed in detail here. It must nevertheless be mentioned that the so-called *vésiculette primordiale* which Civatte[11] claims to be the earliest sign of the eczema reaction, and to which also Polak and Mom[11] assign a decisive importance, has not been observed by Miescher[11] who in his experiments, employed patch tests on allergics with non-toxic substances such as quinine. Miescher[1] found that the histological changes in the epidermis always commenced in the deep layers and later made their way up towards the surface; and he also found lymphocyte immigration to be a very early sign.

Histologically it is hardly possible to decide with certainty on the primary point of origin of *the eczema reaction but this problem* may also be elucidated in other ways, namely experimentally and clinically

Here it is first to be *established that eczematous allergy is, at* any rate, not limited to the epidermis alone, but also involves the corium The proof of this is found in the so-called intracutaneous reactions that can be induced in most eczema allergies. When for instance, a patient with nickel allergy is given an intracutaneous injection of 0 1 ml of a 0 1 per cent (or even weaker) solution of a nickel salt a red infiltrated papule will appear after about twenty-four hours this resembles a positive tuberculin reaction not only *macroscopically but also in its course and its histological features.*

Corresponding reactions may be produced with salts of chrome and mercury—and generally with most soluble antigens—in persons *who give an eczematous reaction to the respective substances by* patch test. It may also be mentioned that these reactions are, as a rule, entirely papular—*i.e* not accompanied by eczematous changes *Only in exceptional cases is an eczematous reaction seen* around the puncture, presumably because the substance has here been in direct contact with the epidermis

Thus the intracutaneous reactions plainly show that the corium is also an organ which reacts in the particular form of allergy we designate as eczematous But as these reactions normally are not accompanied by eczematous changes, although the subcutaneously injected substances presumably will diffuse upwards and reach the *lower layers of the epidermis, it appears as if the eliciting of the* eczematous reaction requires exposure to a substance from the outside, extending inwards. In other words it appears to be a *question of two different forms of reaction* an epidermal and dermal even though most often they may combine into an apparent entity

This is exactly what clinical observations confirm Thus in his studies on turpentine allergy Rokstad found some patients to react chiefly "*epidermally*" *(i e with vesiculation)* whereas in other patients hyperaemia and infiltration—that is th "dermal component—were the more conspicuous features When a fairly *large number* of patch tests and intracutaneous tests are performed simultaneously on eczematous allergics a considerable difference in the sensitivity *may likewise be ascertained* some patients showing a markedly more "epidermal" sensitivity than "dermal" and

vice versa. As emphasized by Epstein[44] the sensitivity is seen to be limited either to the epidermis alone or to the corium.

Generally the intracutaneous reactions are more sensitive than patch tests, which probably is attributable in part to the mode of application. Sometimes the sensitivity is very great. Thus, in a case of chrome eczema, the author was able to demonstrate a positive intracutaneous reaction even to 0.1 ml. of a bichromate solution of 1/1,000,000—a sensitivity exceeding all the usually recognised chemical reactions.

DEMONSTRATION OF HYPERSENSITIVENESS IN ALLERGIC ECZEMA

False Positive Reactions. The method most commonly used in the diagnosis of allergic eczema is the patch test, whose technique has been described in Chapter II.

In the reading of patch tests sources of error are numerous. For one thing, it must be remembered that a patch test is only an *imperfect imitation* of the conditions under which the suspected substance has produced the presenting eczema. In particular, the duration of contact with the suspected substance will often be considerably shorter than the patient's preceding exposure and a negative result, therefore, will not exclude the causative rôle of the substance employed. Rattner[1] has tried to meet this difficulty by means of a special celluloid chamber that can remain on the skin for several days, and in which the test solution can be renewed repeatedly.

More important, however, are the sources of error giving rise to false positive reactions. The concentration of the test solution is of great significance in this respect, as several of the substances which commonly give rise to allergic eczema have a direct toxic effect on the skin when employed in relatively high concentrations. This applies, for instance, to turpentine and many metal salts. Even though such a toxic reaction differs in several respects from a true allergic reaction and can most often be differentiated from the latter by the expert examiner, it is still important to keep the concentration of the test solutions below the toxic limit.

Attempts have been made to establish this limit experimentally on normal subjects,* but the results obtained in this way are not directly applicable to eczematous patients. In the first place, as might be expected, the skin of eczematous patients is less resistant

* See Chapter II, and Appendix A.

to the direct toxic effect. Sometimes, moreover it will also present a true eczematous reaction even in the absence of allergy to the test substance employed. The explanation of this type of reaction, which—*in contrast to the toxic*—is designated as the "false positive reaction" is presumably as follows: in many patients, especially those with extensive and acute eczema the skin is in a particular condition—designated by the older authors as *status ec ematicus* —which causes it not to react like normal skin to various irritants, *mechanical or chemical* but with a true eczematous eruption. Now some of the test substances commonly employed have a somewhat irritating effect on the skin even though their concentration may be considerably lower than that required for a toxic reaction Presumably it is this slight irritation which in *status eczematicus* is able —*in a similar way to the Koebner scratch in psoriasis—to provoke* the eczematous eruption which, so to speak is present in latent form. These "false positive reactions" are indeed generally seen on application of the substances which are known from experience to have the strongest capacity for non-specific irritation especially turpentine, chromates and mercuric salts.

As "false positive reactions," unlike the toxic cannot thus be distinguished offhand from true allergic reactions, they may very easily give rise to misinterpretations. In extensive and acute eczema the positive patch test should be estimated very cautiously especially in cases where directly irritating substances are concerned In the writer s opinion furthermore, patch tests should not be applied *in the vicinity of the eczematous eruption even though in this way* a stronger allergic reaction may be obtained here than elsewhere on the skin for such a procedure implies also a considerable risk of a false positive reaction "

The technique commonly employed for the application of patch *tests involves various drawbacks the most important of which* in practice is the frequent occurrence of irritation produced by the adhesive tape, which may sometimes even completely mask the reactions. In such cases zinc-gelatine or other adhesives have to be used.

In the so-called electrophoretic patch test—which is suitable only for metal salts and other dissociated compounds—the substances or rather the active *ions are introduced into the skin by means of the* galvanic current The amount of the substance thus introduced can here be regulated far more accurately than with patch tests. This method further offers the advantage that the test area is altogether

uncovered, on which account the reaction can be observed throughout its development, and the influence of various factors upon this process can be examined. So even though the electrophoretic patch test is rather circumstantial for diagnosis in clinical practice, it is of great value in research work. By means of this method, for instance, it has been shown that local introduction into the skin of the so-called antihistaminics has no influence upon the allergic eczema reaction.

SPECIFICITY

Allergic eczema reactions are highly specific, probably to about the same degree as serological antigen-antibody reactions. The fact that the antigens are usually fairly simple chemical compounds affords a good opportunity of studying which factors determine specificity. Metal salts are probably the simplest antigens and two of the metals, nickel and cobalt, are so closely related that hypersensitiveness to one of them is not infrequently accompanied by hypersensitiveness to the other. It should be noted, however, that cases of nickel and cobalt eczema encountered in practice do not furnish strict proof of this, as the nickel salts employed in industry usually contain some cobalt and *vice versa*. Nevertheless, overlapping of the reaction has also been demonstrated in sensitization with the pure salts, although the homologous antigen always has the stronger effect.

Interesting information has further been obtained by sensitization with organic compounds—in particular the various dinitrochlorbenzenes, six of which are isomeric. Thus, on sensitization with the 2 4 compound, Rostenberg and Kanof[19] found that the homologous compound always gave the strongest reaction, then the 2 5 and 3 4 compounds, then the 2 3 and 2 6, while 3 5 gave the weakest reaction. Considering the constitutional formulas of the isomers concerned, it at once becomes obvious that specificity decreases with increasing deviation of the substitutes from the 2 4 linkage. Substitution of the chlorine atom with bromine or iodine did not noticeably alter the specificity whereas this was lost on substitution with NH Substitution of NO with Cl gave a considerable fall in the reactivity and the capacity for reaction disappeared completely on removal of one of the NO groups.

The experiments with organic compounds show clearly that the molecular structure is of decisive significance to the specificity whereas the individual components may be replaced, at any rate with closely related ones, without any particular change in the specificity

to the direct toxic effect. Sometimes, moreover it will also present a true eczematous reaction even in the absence of allergy to the test substance employed The explanation of this type of reaction, which—in contrast to the toxic—is designated as the "false positive reaction" is presumably as follows: in many patients, especially those with extensive and acute eczema the skin is in a particular condition—designated by the older authors as *status eczematicus* —which causes it not to react like normal skin to various irritants, mechanical or chemical but with a true eczematous eruption. Now some of the test substances commonly employed have a somewhat irritating effect on the skin even though their concentration may be considerably lower than that required for a toxic reaction Presumably it is this slight irritation which in *status eczematicus* is able —in a similar way to the Koebner scratch in psoriasis—to provoke the eczematous eruption which so to speak, is present in latent form. These "false positive reactions" are indeed generally seen on application of the substances which are known from experience to have the strongest capacity for non-specific irritation, especially turpentine, chromates and mercuric salts

As "false positive reactions" unlike the toxic cannot thus be distinguished offhand from true allergic reactions they may very easily give rise to misinterpretations In extensive and acute eczema the positive patch test should be estimated very cautiously especially in cases where directly irritating substances are concerned In the writer's opinion, furthermore, patch tests should not be applied in the vicinity of the eczematous eruption even though in this way a stronger allergic reaction may be obtained here than elsewhere on the skin for such a procedure implies also a considerable risk of a "false positive reaction."

The technique commonly employed for the application of patch tests involves various drawbacks the most important of which in practice is the frequent occurrence of irritation produced by the adhesive tape, which may sometimes even completely mask the reactions In such cases zinc-gelatine or other adhesives have to be used.

In the so-called electrophoretic patch test—which is suitable only for metal salts and other dissociated compounds—the substances or rather the active ions are introduced into the skin by means of the galvanic current. The amount of the substance thus introduced can here be regulated far more accurately than with patch tests. This method further offers the advantage that the test area is altogether

known from other fields) Accordingly in a sensitized individual an eczematous reaction might then be elicited not only by exposure to the chemical substance but also by substances in the skin itself whenever and however these are liberated.

This hypotheses offers an explanation of various clinical and experimental observations—*e g* eczematous eruption after non-specific irritation in cases of allergic eczema secondary " -id " on the palms in primary allergic eczema of the soles (special cutaneous proteins in these regions) the frequent differences in epidermal and dermal reactivity and the frequently protracted course of eczema produced by substances with marked affinity for proteins (chrome, formalin and many others)

Finally this hypothesis may bring certain forms of eczema hitherto considered non-allergic into the field of allergy For it may be that chemical substances such as alkalies, which are not themselves sensitizing agents and yet give rise to eczema, may perhaps induce this effect by altering cutaneous protein and forming a sensitizing protigen " Presumably the interesting phenomenon designated as auto-eczematization —first described by Whitfield —is to be interpreted in a similar way It comprises eczematous reactions appearing especially as " -id "-like eruptions after non-specifi irritation of varicose eczema, it might be due to " protigens " formed locally in skin altered by stasis, and in this process bacteria may play a contributory part.

Nevertheless, the adoption of this hypothesis meets with certain difficulties. Thus, if the protigens really are of protein nature, one would expect them to appear as " complete antigens," *i.e* giving rise to antibodies of the same character as those encountered in anaphylaxis and immediate reactions on the skin. It may be, however that certain radicles in the " protigen " of similar nature to a simple chemical substance, convey the specificity while the rest of the protein molecule merely acts as " carrier "

As yet it has not been practicable to isolate "*protigens*," but indirect support of their occurrence has been found in clinical observations (Whitfield Brown[44] Smith[44]) serological investigations (Templeton, Lunsford and Allington[44]) and, not least, in positive cutaneous reactions with extracts of scales (Hopkins and Burky Cormia and Esplin Simon)

Besides the still *hypothetical* protigens," we have also to take into account the bacteria and fungi occurring on the skin that may take part in the sensitizing processes—possibly by simply forming

In practice however in cases of allergic eczema encountered clinically specificity varies widely in different patients. This is shown for instance, by numerous studies on the three isomeric divalent phenols (pyrocatechin resorcinol and hydroquinone) where hypersensitiveness is sometimes limited to one and sometimes includes one or both of the other isomers

SIGNIFICANCE OF "PROTIGENS" AND MICRO-ORGANISMS IN ALLERGIC ECZEMA

Even though it were possible to demonstrate antibodies to a simple chemical compound producing allergic eczema the clinical picture and course of such cases can scarcely be explained completely as resulting exclusively from an antigen-antibody reaction of this nature That certain complicating processes are bound to play a part here is evident from numerous observations as, for instance the rapid and benign course of primula eczema as compared with chrome or formalin eczema the production of an eczematous eruption by non-specific simple irritation of the skin in many cases of allergic eczema and finally the peculiar secondary eruptions of the "id" type with their variable, often characteristic, localization*

It has long been assumed that here we might be dealing with sensitizing processes arising from the proteins of the skin which are assumed to alter under exposure to many sensitizing substances. Furthermore, various observations indicate that such sensitization with products originating from the skin itself really occurs.

In an interesting paper based upon his own observations and those reported by other investigators Epstein has advanced a hypothesis which undoubtedly deserves attention its main features being as follows. when the skin is painted with a sensitizing substance we assume that the linkage of this substance with protein results in an antigen having a sensitizing effect. Previously however particular significance was attached to the chemical substance itself while the protein component largely was looked upon as a necessary carrier" In contrast hereto Epstein emphasizes that the protein component is also probably altered in such a way as to have an antigenic effect by itself This antigenic protein compound —which Epstein designates as "protigen"—is assumed to induce the production of one or more antibodies which possibly may react also with normal skin protein (analogies with such overlapping are

* For fuller discussion of this last phenomenon see Chapter IX Ed

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"protigens" Bacterial products appear under certain circumstances to be able to complete substances which by themselves have no antigenic effect. Thus Hecht, Sulzberger and Weil[14] were able to produce *precipitins against rabbit skin* by injecting an extract of the skin plus staphylococcus toxin into rabbits while the extract or the toxin alone was inactive So it seems not altogether improbable that for instance the staphylococci present on eczematous skin may act as an adjuvant in the formation of "protigens" in the skin, besides very possibly exerting an antigenic effect by themselves. This question is difficult to decide however as epicutaneous as well as intracutaneous tests with bacterial products of this kind have given variable results

Work performed at Miescher's clinic, however tends to support this hypothesis and is presented in Chapter VII by Storck who has been particularly interested in this problem. *Ed.*

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3 A greater than normal susceptibility to develop passive transfer antibodies in the blood serum (Prausnitz-Küstner antibodies; atopic reagins)

4 A tendency to develop blood eosinophilia.

5 A susceptibility to other immunologic, autonomic vasomotor and endocrinologic abnormalities leading to consistent aberrations from the norm in response to a variety of stresses (heat, cold, moisture, trauma, emotional tensions, infections,* etc.)

Thus the term "atopic dermatitis" is based on considerations which recognize the basic relationship of the skin lesions to other atopic manifestations. And in addition it makes an effort to embrace possible mechanisms, hereditary features, characteristic immunologic and other laboratory findings, associated conditions of other organs, etc., which the older and other currently used terms did not attempt to include

By definition then, *atopic dermatitis* is that group of inflammatory dermatoses which is characteristically associated with the distinctive phenomena of *atopy* in the affected individual and/or his family In addition to the cardinal manifestations of atopy (*see* above) there are certain rather characteristic features of the skin involvement, each of which will be elaborated upon later These are:

1 The frequent existence of three separate stages: (a) an infantile stage; (b) a childhood stage and (c) an adolescent and youthful adult stage of the disease.

2 The rather characteristic clinical picture which is seen in most cases.

3 The seasonal variations and exacerbations.

4 The almost predictable pattern of response to patch, scratch and intracutaneous testing; the aberrations of sweating; the abnormal cutaneous responses to cholinergic drugs; to stroking; to pressure etc

Under the above definition of atopic dermatitis are included those eruptions variously referred to by such names as "infantile eczema," generalized neurodermite" (Brocq) "prurigo diathésique" (Besnier) "lichen chronicus simplex disseminatus" (Vidal) früh und spaeth exsudatives Ekzematoid" ("early and late

* This susceptibility to infection also shows certain degree of specificity i.e. to the herpes simplex and vaccinia viruses. The characteristic virus-induced vesiculo-pustular eruptions which occur not only in patients with atopic dermatitis, but also with other manifestations of atopy have commonly been referred to Kaposi varicelliform eruption.

5

CHAPTER IV

ATOPIC DERMATITIS

MARION B SULZBERGER and VICTOR H WITTEN

THERE is nothing new in the concept that there is an intimate association between asthma hay fever and certain skin diseases, such as infantile eczema prurigos and disseminated neurodermatitis. Since all of these diseases are characterized by the common presence of the manifestations of "atopy" it is necessary first to be clear as to the meaning of the general term "atopy" as it is employed here, and then to understand the more specific designation atopic dermatitis" as it is being generally accepted and used by physicians

The opinions expressed in this chapter are based on our own experience and it is realized that the statements and conclusions may not be acceptable to all

The term "atopic dermatitis" can be more easily defined once the meaning of its etymological precursor is understood A. F Coca s original term *atopy* literally means *without place* or more freely *a strange disease or state* and may today be defined as follows.

Atopy designates that complex predisposition which is apparently peculiar to man irregularly transmissible in certain human families in which there are manifest various combinations of the following characteristics.

1 An unusually high familial tendency toward such related states and diseases as hay fever asthma and atopic dermatoses (*e g* infantile eczema prurigo mitis, disseminated neurodermatitis)

2. A tendency to develop a relatively high number of allergic hypersensitivities demonstrable as wheal reactions to scratch or intracutaneous tests with common food and inhalant allergens (*e g* egg white, human dander house dust pollens)

3 A greater than normal susceptibility to develop passive transfer antibodies in the blood serum (Prausnitz-Küstner antibodies; atopic reagins)

✓ 4 A tendency to develop blood eosinophilia.

5 A susceptibility to other immunologic, autonomic, vasomotor and endocrinologic abnormalities leading to consistent aberrations from the norm in response to a variety of stresses (heat, cold, moisture, trauma, emotional tensions, infections,* etc.)

Thus the term "atopic dermatitis" is based on considerations which recognize the basic relationship of the skin lesions to other "atopic" manifestations. And in addition it makes an effort to embrace possible mechanisms, hereditary features, characteristic immunologic and other laboratory findings, associated conditions of other organs, etc., which the older and other currently used terms did not attempt to include.

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3 The seasonal variations and exacerbations.

4 The almost predictable pattern of response to patch, scratch and intracutaneous testing; the aberrations of sweating; the abnormal cutaneous responses to cholinergic drugs; to stroking; to pressure, etc

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exudative eczematoid dermatitis ") (Rost) pruritus with lichenification " "allergic eczema * "atopic eczema hay fever eczema " "flexural eczema " "chronic eczema " "lichenified eczema " etc., etc and more commonly by *English-speaking dermatologists as* "generalized or disseminated neurodermatitis."

INCIDENCE

Atopic skin diseases are among the common dermatoses. They occur principally in *infants, children adolescents and youthful* adults up to about twenty-five years of age Within this age group *atopic dermatoses is* an estimated eighth in order of frequency following close upon eczematous contact-type dermatitis, acute urticaria acne vulgaris, seborrheic dermatoses superficial fungous infections pyodermas and drug eruptions.



FIG. 26
Infantile atopic dermatitis. Typical involvement showing oozing and superficial crusting. Note involvement of extensor surfaces.

Infantile Atopic Dermatitis. The first stage of the cutaneous atopic disease is *almost universally referred* to as "infantile eczema" *At about the* end of the second or beginning of the third month (sometimes even before) the infant begins to develop an erythematous eruption most commonly starting on the cheeks It is not unusual to note a tendency toward an erythematous and scaling involvement of the hairy scalp often referred to as cradle cap *which has persisted since birth The* eruption usually spreads peripherally to involve most of the face. It also "jumps to other parts of the body particularly the outer aspects of the lower part of the legs the forearms, wrists and forehead (Fig 26) The bilateral involvement of the antecubital and popliteal spaces, while it does occur is not as common in the infant as in the older age groups There are occasionally irregular disseminated patches of erythema and occasionally a tendency to the formation of edematous papules While there is a polymorphism of

Obviously entirely distinct from the allergic eczematous dermatitis discussed in Chapter III *Ed*

lesions, the most characteristic and constant of these is a small, red, "juicy-looking" papule. Profuse oozing and then crusting, particularly of the cheeks, is not at all uncommon (Fig. 27) Some authorities hold that these "open" lesions are always secondary But whether primary or secondary the fact is that the infantile form of atopic dermatitis often presents minute fragile vesicles, and crusting; such lesions are rare in older patients. This major morphological difference seen in different age groups should not be interpreted as proof of a fundamental difference in the disease process *

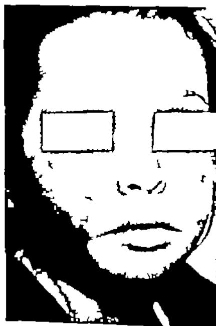


Fig. 27

Atopic dermatitis in the young child. The crusting limited to the cheek is almost diagnostic and is a rather common finding.

* In this connection, it is significant that many dermatoses which are essentially non-vesicular in adults, commonly assume a vesicular or bullous character in infants and young children—e.g. the bullous syphilide of pemphigoid type, vesicular or bullous scabies, bullous impetigo, etc. This suggests that in infants the skin may be more easily penetrated and its superficial layers more easily disrupted than in adults; and thus tends more strongly to the formation of superficial vesicles and bullae. In view of this generally increased tendency to vesiculation and weeping on the part of the infantile skin, as well as in consideration of many immunologic and clinical facts, it is probable that the vesiculation, weeping and crusting seen in the infantile forms of atopic dermatitis is not a fundamental difference between the disease process in infants and adults but a difference in the reactions patterns of infantile and older skins.
(The bullous eruption representing contact eczema in an infant is pictured in Chapter I. *Ed.*)

/ *Most infants with atopic dermatitis recover entirely either before or towards the end of the second year*

However in exceptional instances, infantile atopic dermatitis may become generalized and take on the appearance of erythroderma *These cases with* erythroderma present the most severe and most intractable form of the infantile dermatoses

Atopic Dermatitis of Childhood. The second phase of atopic dermatitis may follow the dermatosis of infancy immediately and without interruption, or the childhood phase may have its onset only several years after an infantile eczema which had disappeared within the first two years of life. In still other cases there is no preceding infantile eczema whatsoever and the skin disease makes its first appearance as the childhood form of atopic dermatitis.

In childhood as contrasted to infancy the cutaneous condition is characterized by *papulation* rather than by vesiculation, exudation and crusting. The childhood form represents a transition between the infantile and adult types and sometimes presents combinations of characteristics and intermediate characteristics. In *this age group the dermatosis commonly assumes one of two forms.* The first is the papular *prurigo* form which consists mainly of *succulent elevated papules with a crusted scratched central top* In this prurigo type, the favored localizations are the *extensor surfaces of the extremities The second is the lichenoid variety* which consists of small discrete, rather flat-topped brown or reddish-*brown papules, becoming confluent in many areas and presenting* lichenoid plaques with indefinite or moderately sharp borders and *outlying discrete, scattered papules* The *flexor* areas, particularly those of the cubital and popliteal spaces, are *favored localizations* in the lichenoid type (Fig. 28)

Not unlike the infantile form atopic dermatitis in the child is usually self limited and may disappear at any time before the age of ten to twelve, either never to recur again or to permit freedom for several years. In other cases the childhood phase may continue uninterruptedly and merge imperceptibly with the succeeding adolescent and adult phase

Atopic Dermatitis of the Adolescent and Adult. The third phase of atopic dermatitis has as its primary dermatologic lesion the papule or a number of confluent papules forming lichenified areas In uncomplicated cases there is no vesiculation and the prurigo form is much less common than in childhood The lichenified plaques formed by the confluent papules are usually drier and

thicker the older the individual, they are not very sharply demarcated and vary in color from a bright pinkish red to a tannish brown or a greyish brown. The lichenified thickened areas are usually surrounded by outlying, scattered and often excoriated



FIG. 28
Atopic dermatitis of childhood. Illustrating transition between infantile form (face) and typical involvement of flexures as found in older individuals. (Compare with Figures 29 and 30.)

papules (Fig. 29). When weeping, crusting and exudation do occur they are usually the result of superimposed external irritation and infection.

In typical cases the distribution is characteristic and often diagnostic (Fig. 30). The favored localization is in the flexures: the

ante-cubital and popliteal spaces, and front and sides of the neck. Other favourite sites are the eyelids, the forehead and scalp the anterior chest, the wrists, the dorsa of the fingers and toes, and the dorsa of the feet In addition to the typical distribution the dermatosis may affect a single area or a few isolated sites or may on the



FIG. 29
Atopic dermatitis of the adult. Showing typical licheni fication with excoriated and crusted papules.

other hand become generalized Thus what appears to be a chronic or chronic recurrent "eczema" of the hands (Fig 31) feet or of the eyelids, or a generalized erythroderma etc., may be a partial or localized form of atopic dermatitis, or a more generalized involvement with exfoliation

In general then it can be stated that the lichenoid papule and the plaques formed by the coalescence of such papules may be considered primary in atopic dermatitis and not only the vesiculation and oozing, but also the superficial infection the thickening of the epidermis the pigmentation and depigmentation and the chronic

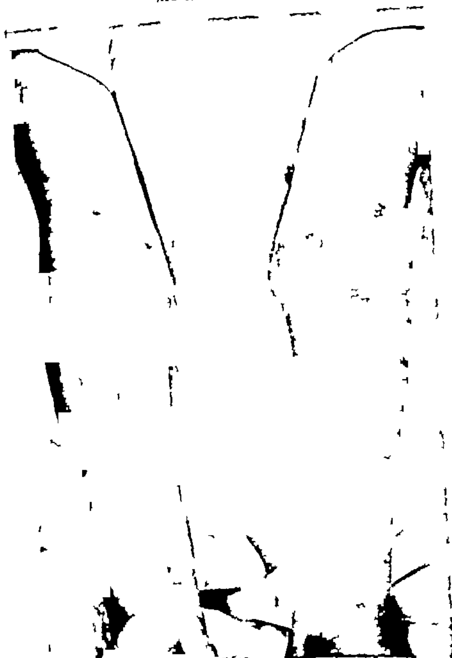


FIG 30

Atopic dermat[illegible] of the adolescent or adult The lichenified thickened involvement of the antecubital spaces (and often the popliteal spaces) together with excoriated and crusted satellite papules are characteristic

diffuse infiltration are secondary *The cardinal lesion of true eczema—the pathognomonic intra-epidermal vesicle—does not constitute a feature of the primary process of atopic dermatitis in the ages beyond infancy*



FIG. 31
Atopic dermatitis involving the hands of an adult When confined to this locality this form may require detailed and prolonged study for differentiation from other eczematous and eczematoid eruptions of the hands.

Pruritus is without question the predominant symptom of atopic dermatitis While the pruritus is extremely variable in its time of occurrence suddenness of onset duration areas involved and intensity almost all patients with atopic dermatitis are certain to suffer the torments and anguish brought on by this the most exasperating and intolerable of all symptoms which plague man One need only see the itching patient literally dig at his skin until it bleeds, or rub with so much pressure as to denude the surface and cause serous oozing or slap and hit the involved part until it swells or see a desperate disoriented sufferer even bang his head

against the bed or wall to appreciate the degree of torture and anguish that an itch-paroxysm can produce.

Fortunately such severity of itching is not consistently present. Nevertheless it is practically the rule for some irritation to occur from scratching or the application of unsuitable medication. Therefore many patients, when first seen, present superficial skin irritations and infections. But, in contrast to certain virus infections (footnote page 65) severe pyodermas and fungous infections are superimposed on the original lesions remarkably rarely considering the continued severe traumas and inoculations imposed on the involved parts.

Associated Findings. In addition to the presence of other atopic diseases, in the majority of patients who have atopic dermatitis there are still other findings which may be elicited in some cases. The most important associated finding, because of its seriousness, should be stressed first—and that is the occasional occurrence of *atopic cataract* which can radically impair vision and even produce blindness. Because of this possibility all cases of severe, chronic atopic dermatitis require careful periodic ophthalmologic examinations.

As far as concerns dermatologic accompaniments it is quite usual to see patients with atopic dermatitis who have skin that is generally dry and rough with areas of follicular hyperkeratosis.

An interesting, important and perhaps fundamental dermatologic observation is the "white dermographism" which is easily produced by stroking the involved skin. This finding is certainly a common characteristic though not necessarily pathognomonic. Furthermore, it is not unusual to see areas of skin, predominantly in the "flush areas" (face, neck and upper chest) suddenly blanch in one small area and rather rapidly spread centrifugally to involve larger areas. This "white dermographism" may perhaps take place spontaneously without visible stimulation to the skin's surface.

Careful questioning and observation will often reveal that the patient with atopic dermatitis does not sweat normally from various areas. Additional study will usually show that the sweat glands in these areas are occluded. Such findings could very naturally account for the abnormal response and intolerance to high temperatures and humidities and perhaps for the symptoms precipitated by sudden changes in temperature, exercise, emotional stresses, etc.

Course of the Dermatosis. In many patients the infantile, childhood and adolescent phases of atopic dermatitis are sharply separated

diffuse infiltration are secondary *The cardinal lesion of true eczema —the pathognomonic intra-epidermal vesicle—does not constitute a feature of the primary process of atopic dermatitis in the ages beyond infancy*

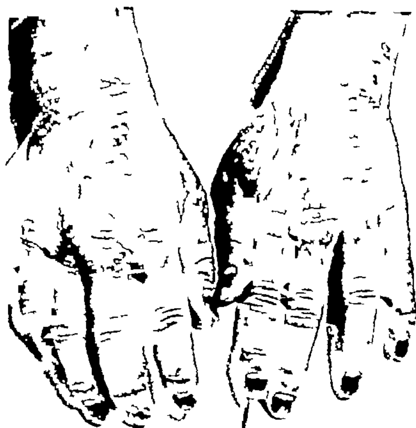


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5. Ingestion of certain foods, notably fish, eggs, wheat, milk and chocolate; and exposure to other allergens, including dusts, vapours and drugs (salicylates, barbiturates, etc.)

6. Specific articles of clothing, such as certain silk, wool or satin garments.

7. Intercurrent infections, particularly the common cold and herpes simplex.*

8. Application of occlusive or "heating" topical medications in the form of grease or greasy ointments.

9. Alkaline agents, including soap and other cleansers.

10. Overwork, "worry" nerves and emotional upsets, fatigue and stress."*

It must be emphasized that although the mass of clinical evidence as to these and other "trigger effects" is impressive, conclusive proof that *any one of them is the primary or sole cause* of the dermatosis is *still lacking*. Nevertheless management of atopic dermatitis must take all such causal or contributory factors into consideration. Any case refractory to the more direct and often simpler measures (*e.g.* topical medicaments) must be attacked by the most thorough elimination of suspected contributory factors such as those listed above.

Office Procedures of Diagnostic Aid. While there are no test reactions which in and of themselves are pathognomonic of atopic dermatitis, there are certain characteristic responses and certain studies which can help in establishing the diagnosis. It must be emphasized at this point, however that a resourceful indefatigable and detailed search for a family and/or personal history of atopy together with the recognition of the characteristic clinical picture are the most important steps in establishing the diagnosis.

The following studies can be done in the office in most instances:

1. Scratch and Intracutaneous Tests. The incidence of positive urticarial reactions to these methods of skin testing with various food and environmental allergens is unusually high. Because of the strong and polyvalent urticarial skin-test hypersensitivity in this group of patients, all the necessary and proper precautions in skin testing must be observed.

Atopic dermatitis of infancy has long been known to be characterized by a tremendously high incidence of positive wheal reactions

* Contrariwise certain febrile infections (pneumonias, typhoid, etc.), many surgical operations and many other non-specific stresses may bring on remissions of various degrees and duration. (Cortisone-like effect?).

from each other by intervals of more or less complete *freedom* In other instances two or all three forms run one into each other without intervals of remission As a rule, all forms of atopic dermatitis terminate in spontaneous recovery Unfortunately there are notable exceptions and one sees an occasional patient over thirty who still presents the most intractable and gravest forms of the dermatosis

Exacerbations and Remissions. Because of the erratic course, with often inexplicable *spontaneous remissions, exacerbations and "cures,"* it is not easy to state the prognosis or to evaluate therapeutic procedures *in atopic dermatitis*

Adequate local therapy (*see* section on Management of Atopic Dermatitis in Chapter XIII) *often contributes to periods of remissions* As a rule the correct local treatment and general management, together with elimination of *offending food and inhalant allergens*, of physical and chemical irritants and prevention of scratching, will result in periods of freedom and often permanent relief—particularly in youthful patients.

In quite a few cases the generally irregular unpredictable recurrences are supplanted by exacerbations which are periodic, often indeed distinctly seasonal In our experience, there is a small group which "flares up" in early Spring and Summer and a much larger group with exacerbations occurring quite regularly in August and September and particularly in October These cases usually clear up within several months, only to recur at the same season the following year Many observers have long suspected seasonal inhalants as possibly decisive trigger factors in these cases and the studies of our School and of Warren Vaughn Louis Tuft, Rowe and others have brought considerable support to this theory without proving it completely

In active atopic dermatoses of all sorts rapid almost hourly variations in the severity of both subjective and objective manifestations are the rule

Exacerbations of longer or shorter duration are often brought about by the following factors

1 Heat, humidity and effort.

2 Cold and wind

3 Rapid changes *of environmental temperature*

4 Perspiration (or attempts to perspire *i.e* the secretion of sweat *without being able to pour it out on the skin's surface*—"sweat retention" internal sweating")

Character of excitant		Water or oil-soluble simple compounds (non-proteins), e.g. dyes, medicaments, etc., products of plants (in oily fraction), etc., products of fungi, etc.	Ingested or inhaled substances, commonly either proteins in nature or associated with proteins (sometimes elicited by external contact, probably through trans-epidermal penetration). Humidity, heat, cold, infections, emotions can act as triggers.	Not known
Antibodies		None conclusively or regularly demonstrated.	Prausnitz-Küstner—passive transfer antibodies common.	None demonstrated.
Eosinophilia		Negat i.e. of normal incidence.	Positive i.e. of abnormally high incidence.	Negative. i.e. of normal incidence.
Results of skin test	Immediate whealing reactions to scratch or intracutaneous tests.	Negative: i.e. of normal incidence.	Positive: i.e. of abnormally high incidence.	Negative i.e. of normal incidence.
	Eczematous reactions after 4-48 hr to patch tests.	Positive: i.e. of abnormally high incidence.	Negative: i.e., of normal or perhaps even subnormal incidence.	Undetermined.

Combinations of any two or of all three forms occur. The most common combination is that of seborrheic and atopic dermatitis.

The combined forms present the combined characteristics of the forms concerned.

From Sulzberger: Dermatologic Allergy (Springfield, Ill: Charles C. Thomas, Publisher 1940).

TABLE I

DIFFERENTIAL DIAGNOSIS OF CONTACT TYPE ALLERGIC ECZEMATOUS DERMATITIS, ATOPIC DERMATITIS AND SEBORRHEIC DERMATITIS*

	CONTACT TYPE DERMATITIS (ECZEMA)	ATOPIC DERMATITIS	SEBORRHEIC DERMATITIS
Age of onset.	Any age not usually preceded by infantile eczema more common in adults.	Often preceded by infantile eczema " often then appears in two later phases: (1) childhood, *6-10* years; (?) adolescent and adult form, 13 30 years.	Late childhood, early adolescence or any time thereafter perhaps sometimes preceded by seborrheic type of infantile eczema (?)
Familial and personal history of atopic diseases (hay fever asthma, infantile eczema").	Negative *i.e* of normal incidence.	Positive. *i.e* of abnormally high incidence in both family and personal history	Negative *i.e* of normal incidence.
Familial and personal history of seborrheic conditions.	Negative i.e of normal incidence.	Negative i.e., of normal incidence.	Positive *i.e.*, abnormally high incidence of male type of baldness, dandruff acne vulgaris, greasy and oily skins, patulous follicles (" kerose").
General appearance of skin outside of affected sites.	Usually normal sometimes excessively moist, dry greasy or keratotic.	Often dry with tendency to hyper pigmentation and follicular keratosis.	In some cases, tendency to greasy and/or oily skin, but often normal in appearance
Common characteristics f eruption.	Not sharply demarcated, acute or subacute, usually moderately pruritic dermatosis, consisti g of one or m re of the f llowing: erythema, edema, vesicles, bullae, papules, scall g, infiltration and lichenification. Usually onset or incipal involvement occurs on the [illegible] areas.	Papular lichenified, highly pruritic, not sharply demarcated with predilection for cubital a d popliteal spaces, eyelids, sides of neck dorsa of hands nd fingers.	Diffuse or sharply circumscribed, *erythematous*, *non-blistering*, superficial scaling dermatitis, with little or no itching. Scales re usually greasy as can be demonstrated by rubbi g between folds of pape Fa ourit sites, scalp for sead, gles of nose, [illegible] ove at ruum

TABLE II

TWENTY PATCH TEST SUBSTANCES SELECTED FOR USE IN DIFFERENTIAL DIAGNOSIS*

1. Whitfield's ointment, N.F. Petrolatum āā.
2. Turpentine, 50 per cent. in olive oil.
3. Sodium arsenate, 1 per cent. aqueous solution.
4. Neoarsphenamine, 1:500 aqueous solution.
5. Milled pyrethrum, as commercially obtainable (water added to make thick paste).
6. Butesin picrate, 5 per cent. ointment as commercially obtainable.
7. Quinine hydrochloride, 1 per cent. aqueous solution.
8. Resorcin, 1 per cent. alcoholic solution.
9. Paraphenylenediamine, 2 per cent. in petrolatum.
10. Tuberculin, 1:1,000 in physiologic saline.
11. Trichophytin, 1:1,000 in physiologic saline.
12. Potassium iodide, 25 per cent. in lanolin-petrolatum āā.
13. Formalin, 5 per cent. aqueous solution.
14. Nickel sulphate, 5 per cent. aqueous solution.
15. (a) Bichloride of mercury 1:1,000 aqueous solution or (b) 5 per cent. [illegible] ammoniated mercury ointment.
16. Tetrabromfluorescein (powder—water added to make thick paste).
17. Sudan III, 5 per cent. in olive oil.
18. Poison ivy acetone extract (8-13 per cent. solids), diluted 1:5,000 with acetone.
19. Ammonium fluoride, 1 per cent. aqueous solution.
20. Benzocaine, 5 per cent. in lanolin-petrolatum āā.

TABLE III—EXTRACTS FOR ROUTINE SCRATCH TESTS

A. FOODS (70)

Almond	Cocoa	Mackerel	Potato, white
Apple	Codfish	Milk	Potato, sweet
Asparagus	Coffee	Mustard	Prune
Banana	Corn	Oat	Rhubarb
Barley	Crab	Onion	Rice
Bean	Duck	Orange	Rye
Beef	Egg white	Oyster	Salmon
Beet	Egg yolk	Paprika	Sole
Bluefish	Garlic	Pea	Spinach
Cabbage	Grape	Peach	Strawberry
Carrot	Grapefruit	Peanut	Tea
Casein	Halibut	Pear	Tomato
Cauliflower	Herring	Pecan	Tuna fish
Celery	Lamb	Pepper, black	Turkey
American Cheese	Lemon	Pepper (red and green)	Veal
Chestnut	Lettuce	Pineapple	Wheat
Chicken	Lima bean	Pork	Whitefish
Clam	Lobster		

B. INHALANTS (17)

Camel hair	Goat hair
Cat hair	Horse dander
Cattle hair	Kapok
Chicken feathers	Orris root
Cotton	Rabbit hair
Dog hair	Sheep wool
Duck feathers	Silk
Dust	Tobacco
Goose feathers	

* From Sulzberger, Dermatologic Allergy (Springfield, Ill.: Charles C. Thomas, Publisher, 1940).

to skin tests with egg white. Moreover Storm van Leeuwen *demonstrated a particularly high incidence* of positive wheal reactions to intracutaneous testing with *extract of human dander in* adult atopic patients (asthma hay fever) and these findings have been confirmed by many others as applicable in fullest measure to atopic dermatitis as well *In recent years the reactions of atopic* dermatitis to human dander applied by various kinds of skin tests (patch scratch intracutaneous) have received particular emphasis through *the careful and precise investigations* of Frank A. Simon.

2 PATCH TESTS In *patients with atopic dermatitis there is* usually a *normal or less than normal* incidence of typical eczematous reactions to patch tests. An exception to this statement however *is the relatively high incidence of papulo-pustular reactions to patch* tests with certain metallic salts (*e g.*, nickel sulphate, arsenicals, iodides) and to certain proteins (*e g* danders, silk) *

3 BLOOD COUNTS There is a moderate to marked eosinophilia in over 50 per cent. of cases

4 DERMOGRAPHISM White dermographism is the rule when the affected areas are firmly stroked.

5 " PASSIVE TRANSFER TESTS This method of testing is *intentionally mentioned last in that it is not ordinarily an office* procedure. In general most atopic patients giving positive wheal reactions to allergens also have passive transfer antibodies (*i.e* atopic reagins) in their blood sera

It must be stressed that when we perform skin tests in suspected atopic dermatitis we often do so *not primarily to ascertain the causes* of the disease in the particular individual but to *gain information which may be of differential diagnostic value* Table I sets forth briefly the salient points of differential diagnosis, based on the history clinical characteristics, skin tests, laboratory examinations and other procedures.

Tables II and III give lists of substances which may be used in differential diagnostic skin testing

Clinically and especially histologically these reactions can often be differentiated from the characteristic patch test *response of true allergic eczematous* contact dermatitis. Under the microscope instead of the allergic eczematous spongiosis and vesiculation of the stratum mucosum, there is a more superficial corneal and subcorneal primary irritation with ... of inconsiderable leukotaxis. Small areas of superficial etchings and polymorphonuclear infiltrates are to be seen *often beginning at points of the skin's least resistance* to penetration, *i.e* at the upper stretches of the follicula and sweat *duct openings.*

g Medication in general.

1 For headache.
2. For constipation.
3 For "acid" in system
(blood purifiers—tonics)
4 For sleeplessness.
5 For nervousness.
6 For coughs.
7 For menses.
8 Bromo-Quinine Laxative.
9 Bromo-Seltzer
10 Iodized salt.
11 Antihistamines
(elicit all by name)
12. Hormones.
13 Vitamins.
14 All other medications (proprietary or prescribed by internal or external routes)

h Cosmetics.

1 Used by you (lipsticks, nail lacquers, scalp tonics, wavesets, powder rouge, perfumes creams, freckle creams, wrinkle removers, deodorants, massages, etc.)
2. Used by others in home.
3 Applied at beauty parlor or elsewhere.

i. Occupational and avocational exposures.

1 At work.
(i) Substances handled.
(ii) Incidental substances handled—*e.g* cleansers.
(iii) Physical conditions of the contacts.
2. At home.
(i) Cleansers, insecticides (professional exterminators)
(ii) Pets, plants, substances used in their care.
(iii) Physical conditions of the contacts.
(iv) Hobbies—photography woodwork, stamp-collecting, etc.
(v) Miscellaneous.

In summary the evaluation of the history and of the differential diagnostic skin tests is based on three points.

TABLE III (*Contd.*)

C. PLANTS AND POLLENS (16)

Blue grass	Plantain
Cocklebur	Ragweed, giant
Corn	Ragweed, short
Dahlia	Redtop
Dandelion	Rose
Goldenrod	Rye
Marsh elder	Sumac
Orchard grass	Timothy

The following questionnaire may prove helpful in history taking:

I. Have you or has anyone in your family had
 - *a* Asthma
 - *b* Hay fever or vasomotor rhinitis (seasonal occurrences)
 - *c* Infantile eczema.
 - *d* Atopic dermatitis (neurodermatitis disseminata or infantile eczema)
 - *e* Seborrhea
   1. Dandruff
   2. Acne.
   3. Falling hair—baldness
 - *f* Hives—angioneurotic edema
 - *g* Fungous infections or other skin eruptions
 - *h* Idiosyncrasy to drugs.
 - *i* Other familial diseases

II
 - *a* When did eruption begin?
 - *b* Was there a similar previous attack?
 - *c* Where did the eruption begin and how did it spread?
 - *d* Is it constant or periodic? of sudden onset?
   1. Seasonal influences.
   2. Other chronologic association with home or other contacts
   3. Other remarks on course of malady
 - *e* Do you know of anything which makes your skin trouble worse?
   1. Foods
   2. Clothing.
   3. Menses
   4. Illnesses and remedies
   5. Miscellaneous
 - *f* What have you done for it—internal and external medicaments and treatments?

2. Lichen planus, in unusual and atypical forms, sometimes presents difficulties. The absence of atopy is again of help in differentiation. It is, however of greatest importance to find the typical papules of lichen planus, which are polygonal in shape with a flat, shiny top and have a violaceous or dull crimson hue. The characteristic involvement of the mucous membranes is also pathognomonic for lichen planus. The histopathology in this disorder is often conclusive.

3 Dermatitis herpetiformis, even though extensive, usually presents evidence of grouping of lesions and other characteristic distinguishing features, such as the age of the patient, course of the disease and presence of vesicles or bullae. The lesions are very frequently polymorphous and the subjective symptoms are usually more those of burning than of itching.

4 Nummular eczema can appear at any age and affects both sexes about equally Coin-like (nummular) plaques are made up of pinhead-sized papules and papulovesicles which often become grouped and then confluent. The plaques may vary in size and number and can appear on any part of the skin. The favoured localizations however are the dorsa of the hands, extensor surfaces of the arms and extensor and outer aspects of th legs and thighs.

5 The prurigos occasionally must be differentiated, although the prurigo mitis is often correctly considered as one of the atopic dermatoses because of the associated atopy Prurigo of Hebra is sometimes considered as an example of an atopic dermatosis. It is classically described as commonly beginning in infancy or early childhood, continuing through life, and characterized early by urticarial lesions and later by markedly pruritic minute papules on the extensor surface of the extremities, as well as the trunk (see Atopic Dermatitis in Childhood)

6. Other chronic itching, lichenified dermatoses, including tinea cruris and pruritic chronic plaques of psoriasis, lichen amyloidosus, etc.

7 Also to be ruled out, particularly in the adult, are the generalized exfoliative dermatides, including psoriatic erythroderma, pityriasis rubra, pityriasis rubra pilaris, etc.

•

1 When the family and personal histories are positive for atopic diseases and there are *several positive immediate wheal reactions* to scratch or intracutaneous tests and negative reactions to the routine patch tests, *this speaks in favour of the diagnosis of atopic dermatitis*

2. When *the family* and personal histories are essentially negative for atopic diseases and there are several positive reactions *to the routine* patch tests and no reactions to scratch or intracutaneous tests the diagnosis of *eczematous contact-type dermatitis is suggested.*

3 Lack of historical or other data indicating the presence of atopy and absence of reactions to either of the two forms of skin tests suggest *seborrheic dermatitis* or *some other dermatosis* as more likely than either atopic or eczematous dermatitis

SPECIAL PROBLEMS OF DIFFERENTIAL DIAGNOSIS

The most difficult problems in differential diagnosis are usually to be found *in older adolescents and adults* *Here one sees atypical* forms combinations with other dermatoses and cases in which *superimposed* secondary *changes often present* difficult diagnostic problems.

But these difficulties are usually not encountered in the infant for the classic easily diagnosed picture of " infantile eczema " *is in the vast majority of cases an example of infantile atopic dermatitis.* It is therefore practical and usually correct for the physician to assume *that an itching eczematoid eruption* of an infant s face and scalp is probably atopic dermatitis Though the problems of diag nosis are most common in regard to differentiation between atopic dermatitis seborrheic dermatitis and contact-type allergic eczematous dermatitis (Table I) the following must also be considered.

1 Lichen chronicus simplex circumscriptus (chronic circumscribed neurodermatitis) which usually appears in fairly sharply circumscribed lichenified plaques As a rule circumscribed lichen simplex involves a single part or at most two or three sites and has its favourite localization on extensor surfaces (*e g* the shin ulnar aspect of the forearm nape of the neck) occasionally on the inner aspect of the thigh or in other regions not characteristically involved by atopic dermatitis. The characteristic appearance and localization at only one or two sites, the items of evidence in the history and particularly the absence of other findings of atopy serve to distinguish this circumscribed form of lichen simplex from atopic dermatitis

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In closing this chapter the following summary may be appropriate:

"Atopic dermatitis" is used *to designate the inflammatory* dermatoses intimately associated with the other characteristic familial atopic aberrations from the norm (*e g* asthma hay fever etc)

These skin eruptions occur characteristically in three phases and are exceedingly common and distressing but are usually (though not always) self limited They run an erratic course with exacerbations which are often seasonal

While allergy of atopic type occurs in over half of these individuals, its exact rôle in the production of the skin lesions is not certain. In many cases dietary and environmental allergens can be proved to cause exacerbations, but other factors do so equally often (cold heat, humidity alkalis, stress)

Dermatologic therapy with properly selected and applied external agents is in and of itself the approach most likely to succeed. However the exclusion of the trigger mechanisms, including elimination of suspected allergens, should not be neglected in cases not responding satisfactorily to direct local treatment Change of environment, especially hospitalization and moving to dry warm, even-temperatured climates is most often beneficial This suggests, among many other things, the importance which aberrations of *sweating (sweat retention and all its consequences) may* have in the production of the itching and exacerbations.

Management, though often highly successful is generally symptomatic rather than causal or specific The details of management of all forms of atopic dermatitis are discussed elsewhere in this text (Chapter XIII)

It is particularly encouraging and worthy of note that research and investigation in the field of atopic dermatitis has not only continued but newer methods of study are being used by the clinician and in the laboratory Through these studies both the understanding and management of the atopic dermatoses have improved materially during recent years and there is good reason to hope for continued and accelerated progress in the years ahead.

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and push upward a new layer of cells of polyhedral shape which become flattened as they reach the upper part of the epidermis. The surface of these cells is provided with thin spines (prickles) which are connected with adjacent prickle cells, thus forming intercellular bridges. The cytoplasm of these cells also contains numerous fibrils which pass in parallel bundles through the intercellular bridges connecting the cells (tonofibrils) A network is thus formed in the meshes of which the epidermal cells lie.

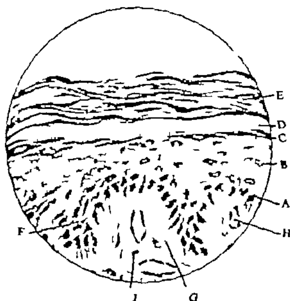


FIG. 32

Normal skin A basal layer B. prickle cell layer (these two layers constitute the stratum Malpighii) C stratum granulosum, D stratum lucidum E stratum corneum, F rete peg, G papilla H capillary J connective tissue cell. Drawing 10. (Miss A. Gretner The Institute of Dermatology)

Stratum Granulosum. Here there are three to four layers of flattened cells of rhomboid shape containing keratohyalin granules, arranged particularly round the nucleus. Keratohyalin is a solid or semi-solid substance, which appears to be related both to keratin and hyalin.

Stratum Lucidum. This layer is seen only in the skin of the palms and soles. It consists of closely packed cells within which no nucleus can be demonstrated. The cells contain an oily substance called eleidin.

CHAPTER V

HISTOPATHOLOGY OF ECZEMA

HENRY HABER

IN conformity with the principle adopted throughout this work no distinction between eczema and dermatitis will be made here.

Eczema is a dynamic process exhibiting lesions which develop from one stage of inflammation to another It begins as an erythema, followed by papules which change into vesicles these dry up to form crusts and when healing takes place desquamation occurs. A patch of eczema will therefore show a composite picture of papules, vesicles, crusts and scales on an erythematous base. This picture may vary with the acuteness of the process and this may in fact be arrested at any stage. The histology will, therefore, vary to a great degree and the histopathologist will be able to state only whether there is an acute, subacute or chronic eczematous condition in each individual case.

NORMAL HISTOLOGY OF THE SKIN

The skin is composed of two principal layers, the epidermis and the underlying dense connective tissue layer called the dermis, cutis or corium Beneath the corium there is a loose connective layer which is transformed into the subcutaneous fat layer in many parts of the body

The epidermis is a stratified squamous epithelium and is most typical on the palms and soles. Four main layers can be distinguished (Fig 32) proceeding towards the surface they are:

1 Stratum Malpighi
2. Stratum granulosum
3 Stratum lucidum.
4 Stratum corneum (horny layer)

Stratum Malpighi. The deeper part is called the basal layer which is next to the cutis and consists of cylindrical cells arranged perpendicularly to the surface of the skin The basal cells multiply

stages of eczema. The first change is the degeneration of a few subcorneal cells and the attraction of histiocytes from the underlying papillary body. There follows a complete disorganization of that area into which fluid passes to form the so-called "*vésiculette primordiale*". The spongiosis is secondary to the vesicle. This primary change takes place both in contact and endogenous eczemas

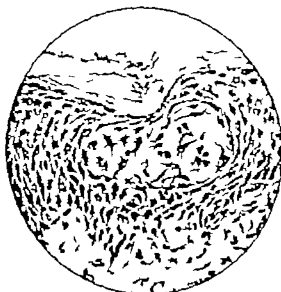


Fig. 33

Marked spongiosis. The prickles are stretched to the utmost. A vesicle is almost formed. Drawing × 210. (Miss A. Gretener, The Institute of Dermatology.)

(Civatte.) Miescher, however, could not confirm Civatte's findings: according to him, the first changes consist of spongiosis in the lower part of the epidermis, accompanied by a mononuclear infiltrate from the inflamed papillary body. As the spongiosis increases vesicles form containing serum, round cells and degenerating epidermal cells. In Miescher's opinion the *vésiculette primordiale* when found, is of toxic or allergic toxic origin.

Percival *et al.* believe that primary localized necrosis and liquefaction of epidermal cells attracts fluid by some physico-chemical force to form a vesicle. This concept is in agreement with Kyrle who postulates a primary anatomical change of the epidermal cells before fluid can disrupt the firm fabric of the stratum Malpighi. Lelour also suggests a primary intracellular oedema (*altération cavitaire*) as the beginning of a vesicle, the cells undergoing

Stratum Corneum The horny layer attains a considerabl thickness on palms and soles and *consists of cornified flattened* cells which contain keratin.

The epidermis contains no blood vessels and is nourished by the tissue fluid which penetrates into the intercellular spaces of the Malpighian layer from the capillaries of the underlying corium.

The Corium is a mesodermal structure made up largely of connective tissue and cellular elements. It is divided, for descriptive purposes into upper middle and deep portions and has at its surface regular digitations, the papillae between which the epidermis dips as " rete pegs The epidermo-dermal junction therefore has a wavy appearance The corium contains muscles, nerves, *the appendages and blood vessels.* Capillaries are *found in the* papillary body and around appendages arterioles are present in the upper cutis and arteries in the deep parts

HISTOPATHOLOGICAL TERMS

Acanthosis means thickening of the stratum Malpighi It is due to the *numerical increase of prickle cells and in eczema* also to intra and intercellular oedema

Hyperkeratosis is thickening of the stratum corneum.

Parakeratosis *designates incomplete keratinization of the stratum* corneum the cells of this layer still containing nuclei It is due to the presence of fluid in the underlying parts and also to a disturbance of normal keratinization as shown by the absence of the stratum granulosum in areas of parakeratosis.

Spongiosis is marked intercellular oedema leading to the production of a spongy appearance of the epidermis. As the fluid from the underlying corium accumulates the prickles are stretched to the utmost and break (Fig. 33) *Small cavities are thus formed which* are filled with fluid these are called *vesicles*

Lichenification is thickening of the skin presenting certain *clinical features*

It is proposed to discuss certain clinical types of eczema from the point of view of the histopathologist

CONTACT DERMATITIS (ECZEMA)

This variety is eminently suitable for the study of the pathology of eczema because it can be produced experimentally and is the chief source of our knowledge of pathological events in the earliest

The stratum Malpighi is only slightly acanthotic and shows inter and intracellular oedema. The striking feature is the appearance of spongiosis leading to the formation of several large vesicles containing coagulated serum and mononuclear cells (Fig. 35). The vesicles are situated in the centre of the stratum Malpighi, but



FIG. 35

Acute contact dermatitis. Characteristic vesiculation, spongiosis and immigration of round cells with mild inflammatory changes in the upper corium. H.E. stain ×104.

there are also several vesicles which lie immediately under the stratum corneum. The deeper parts of the stratum Malpighi also show spongiosis with immigration of lymphocytes; these areas seem to be directly associated with the underlying vessels. The upper cutis is oedematous and shows a very marked peri-vascular infiltration, consisting chiefly of lymphocytes and an occasional eosinophil. The following events may happen:

The vesicles may be ruptured by scratching or eliminated by the normal process of keratinization. Crusts may form and these are thrown off and followed by parakeratosis. If the process is arrested at this stage the skin becomes normal; sometimes only erythema and papules develop and the process may subside again with desquamation. In that case spongiosis and mild inflammation in the papillary body will be seen histologically. If the process is very acute continuous vesiculation and spongiosis take place leading to a disturbance of normal keratinization so that neither

degeneration and leaving a cavity into which fluid passes. Thus vesicle formation follows on either *intra* or *intercellular oedema*. Whether the inflammatory response in the papillary body is primary or secondary to the epidermal change cannot be *stated* as both dermal inflammation and spongiosis are found at the time of micro-



FIG. 34
Acute contact dermatitis On the left a vesicle has formed. On the right there is spongiosis and immigration of round cells. The inflammatory changes in the upper corium are mild H E. stain 34...

scopic examination. Kreibich s[1] theory implies that stimuli acting on the epidermal cell or the nerve endings are conveyed to the peripheral nervous system whence they pass via an axon reflex to the corresponding blood vessels thus producing inflammation and exudation Fluid then invades the intercellular spaces of the epidermis producing first spongiosis then vesiculation If this were so the initial change would be inflammation in the papillary body But it cannot be ascertained whether the stimulus as such could produce primary damage to the epidermis impossible to detect microscopically Kyrle at least postulates such an event.

Whatever the theories may be concerning the formation of an eczematous reaction *the histological picture of an acute contact eczema* whether produced by a primary irritant or by an eczematogenic allergen presents the appearance of spongiosis and vesiculation Figures 34 and 35 illustrate the picture of an acute contact dermatitis. The epidermis shows a loose hyperkeratosis with a few patches of parakeratosis. The stratum granulosum is unchanged

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stratum granulosum nor stratum corneum is formed. The superficial parts of the stratum Malpighi are partly destroyed and the papillae thus denuded, these are the "pits of Devergie." The epidermis has lost its capacity to hold the fluid from the inflamed corium and the affected area weeps freely. Within the corium the inflammatory changes are very marked. After the acute stage has abated the stratum Malpighi becomes thickened and a new stratum granulosum is formed producing first a parakeratotic and then a keratotic layer. This comprises healing.

A Primary Irritant may alter the picture by producing necrosis of the epidermis which ranges from achromia to severe destruction of individual cells. The vesicles are not so numerous and may even be entirely missing. Spongiosis is also present and inflammation in the upper corium is variable. It should be emphasized that intercellular oedema or spongiosis leading to the formation of vesicles is the main feature of an eczematous reaction but does not necessarily imply that it is of allergic origin.*

AUTOSENSITIZATION (DISSEMINATED ECZEMA)

No diagnostic histological features are demonstrable; the picture is that of a mild eczematous eruption.

ATOPIC DERMATITIS

This condition is based on atopic sensitivity, i.e. sensitivity chiefly of the deeper layer of the vascular structure of the skin, and shows positive scratch and intradermal reactions. The commonest type is *Besnier's prurigo*, a chronic dry eczema involving the flexures and face. There is also a moist type of atopic dermatitis called *exudative neurodermatitis* involving the face and the extensor surfaces of the limbs. Lesions consist of sharply circumscribed plaques without vesiculation but considerable exudation and serous crusting. If the lesions extend to thickened parts of the hands and feet they are dyshidrotic in type.

The histology of the dry type of atopic dermatitis differs from that of contact dermatitis. Changes in the epidermis consist of hyperkeratosis with patchy parakeratosis, acanthosis and some spongiosis. The capillaries show oedematous swelling of their wall. The infiltrate in the acute phase consists of polymorphonuclear and

* Many authors, including Haxthausen (Chapter III), emphasize that lymphocytes are increased in the epidermis in allergic contact eczema and granulocytes in primary irritant (toxic) dermatitis. *Ed.*

eosinophil leucocytes and in the chronic stage of lymphocytes, histiocytes, some plasma cells and mast cells; sometimes the eosinophils may reach a proportion of up to 40 per cent.

In the moist type there is hyperkeratosis and parakeratosis, oedema, spongiosis and microscopical vesiculation. Immigration of round cells and polymorphs is seen. The corium is oedematous, with dilatation of the vessels, which are surrounded by round cells, polymorphs and fibroblasts.

ECZEMATIDES (DARIER); SEBORRHOEIC ECZEMA (UNNA)

This group of dermatoses is characterized by erythemato-squamous eruptions exhibiting circinate, psoriasiform and pityriasiform varieties. Some are difficult to distinguish from pityriasis rosea others begin around follicles and spread to form circinate patterns. They show a typical localization in "seborrhoeic areas" (see Chapter VIII) and a tendency to eczematization when they ooze. This fact prompted Darier to call them *eczématides*, and the resemblance to eczema is also seen microscopically. The *eczématides* are identical with Unna's seborrhoeic eczema.

The histology of the dry type of *eczématides* is that of a desquamating dermatitis. There is parakeratosis, acanthosis, mild spongiosis with immigration of round cells and a few polymorphs. The upper corium shows perivascular round cell infiltration with a few polymorphs. In the weeping stage the spongiosis is more marked, minute vesiculation appears and the immigration of round cells and leucocytes is increased. The inflammatory reaction resembles that seen in the dry type. Histologically this condition cannot be distinguished from a subacute or desquamating eczema; it certainly does not show any features of psoriasis, which it may resemble clinically.

ECZEMATOID ERUPTIONS DUE TO FUNGI

Epidermophyton Floccosum produces characteristic scaly patches with a progressing vesicular margin; the disease is known as *eczema marginatum*.

Trichophyton and **Microsporum** species produce vesicular eruptions. Intertriginous eczemas may be due to infection with fungi or may be complicated by them.

stratum granulosum nor stratum corneum is formed. The superficial parts of the stratum Malpighi are partly destroyed and the papillae thus denuded, these are the "pits of Devergie." The epidermis has lost its capacity to hold the fluid from the inflamed corium and the affected area weeps freely. Within the corium the inflammatory changes are very marked. After the acute stage has abated the stratum Malpighi becomes thickened and a new stratum granulosum is formed producing first a parakeratotic and then a keratotic layer. This comprises healing.

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* Many authors, including *Haxthausen (Chapter III)*, emphasize that lymphocytes are increased in the epidermis in allergic contact eczema and granulocytes in *primary irritant (toxic) dermatitis. Ed.*

Figure 36 shows features of a subacute vesicular eczema. The epidermis exhibits desquamation, focal spongiosis and vesiculation. The striking feature is the acanthosis of the interpapillary processes, which have become elongated; they will be seen to branch and fuse. The corium shows a considerable round cell infiltration around dilated blood vessels.



FIG. 36

Vesicular eczema. Hyperkeratosis and parakeratosis, spongiosis and vesiculation. Elongation of rete pegs with branching and fusing. Marked inflammatory changes in the upper corium. H.E. stain × 112.

Figure 37 represents a section taken from a patch of weeping eczema. There is sero-cellular crusting overlying an epidermis which has lost its stratum corneum and granulosum. In one place the stratum Malpighi has also disappeared and a papilla has become denuded. This denuded papilla is clinically expressed by a "pit." The acanthosis is considerable, the spongiosis minimal, and vesiculation non-existent. This picture is, of course, also found in weeping contact dermatitis. The infiltrate in the papillary body is well marked.

Figure 38 is a biopsy taken from an old patch of hyperkeratotic eczema. There is a very marked hyperkeratosis with patchy parakeratosis corresponding with areas of absence of the stratum granulosum. Spongiosis and vesiculation are focal and mild. The acanthosis is considerable and irregular, the rete pegs being greatly

The histopathology of eczematoid eruptions due to fungi is not diagnostic being that of a subacute or chronic dermatitis. There is usually parakeratosis, acanthosis spongiosis and immigration of round cells, with superficial vesiculation The papillary body shows oedema and perivascular round cell infiltration The MacManus method for detecting mucopolysaccharides in tissues may be useful in demonstrating fungi in the epidermis

INFECTIOUS ECZEMATOID DERMATITIS

The title was coined by Engman to designate a vesicular or pustular eczematoid dermatosis which follows on trauma infection or suppurative conditions such as a discharging abscess, a boil or discharging otitis media where the discharge comes in contact with the skin This concept has been considerably broadened as many dermatologists use the term to designate any eczematoid eruption which clinically suggests an infective origin Thus certain cases of nummular eczema fungous infections, infected stasis dermatitis and seborrhoeic intertrigo are covered by this term *

A biopsy from a patch of infectious eczematoid dermatitis shows the following features

There is sero-cellular crusting with superficial vesiculation, acanthosis and immigration of round cells and polymorphs. A characteristic feature is the finding of denuded papillae which are clinically expressed by oozing pits. The papillary body may show considerable oedema [a]

ENDOGENOUS ECZEMA

There still remains a group of eczematous eruptions which do not fit in any group described and are probably of internal origin The histology is that of an eczematous eruption differing from an acute contact dermatitis by reason of its chronicity but presenting substantially the same picture. Vesiculation is not so marked as in acute contact dermatitis but acanthosis is conspicuous The picture may be complicated by episodes of remission and relapse, secondary infection and superimposed contact dermatitis.

It is therefore difficult to obtain a clear picture in each case and the histology will show variations as exemplified by the following three sections:

The classification suggested in Chapt r I would class all these cond tions as microbial eczema", neither clinical nor h st l gical criteria warrant the retention of many of the titles used today *Ed*

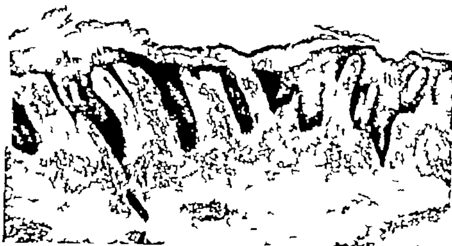


Fig. 37

Weeping eczema. Serocellular crust in the centre. One papilla is denuded. Marked acanthosis with little intercellular oedema and no vesiculation. Inflammatory reaction within the upper corium. H.E. stain × 11.



Fig. 38

Chronic hyperkeratotic eczema. M rked hyperkeratosis, patchy parakeratosis with correspond ng absence of the stratum granulosum acanthosis with considerable downgrowth of elongated and fused rete pegs mild spongiosis and vesiculation Immigration of round cell from the underlying corium, which xh bits oedema d marked chronic nflammation. H.E. stain 11.

elongated as well as branching and fusing. The infiltrate of the upper corium is marked and is partly diffuse and partly perivascular

NUMMULAR ECZEMA

The nature of this condition is still a matter for speculation (see Chapter X). It is variously regarded as an exudative neurodermatitis, infectious eczematoid dermatitis and infective eczema.

Figure 39 shows the histology of a typical patch of nummular eczema. There is a solid layer of stratum corneum overlying a



FIG. 39

Nummular eczema. The stratum corneum is thickened and the stratum granulosum looks normal. The prickle cell layer shows acanthosis with focal spongiosis and vesiculation. There is marked inflammation under the focus. H.E. stain [illegible]

normal stratum granulosum. The stratum Malpighi shows marked regular acanthosis with no oedema. The picture resembles atopic dermatitis, but in the centre of the section two vesicles are apparent, one situated immediately under the stratum corneum, the other above a papilla. There is also some spongiosis and infiltration of round cells. The papillary body shows slight inflammation of the part situated immediately below the spongiosis and vesiculation. If a patch of nummular eczema becomes infected it cannot be distinguished from any other infected eczema.

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Chapter VI

CUTANEOUS RESISTANCE TO ALKALIES, ACIDS AND COMMERCIAL SOLVENTS

W Burckhardt

THE skin is an organ of external protection and consequently comes into contact with numerous harmful substances. These comprise lyes, acids, organic solvents, oxidizing and reducing agents, vegetable poisons and so on. Against these noxae the skin employs physical and chemical defences which vary within certain individual limits and in this way individual variations in resistance are determined. In the first instance such differences in resistance or vulnerability have nothing to do with allergic sensitivity: for example, the subject who suffers from a lowered resistance to lyes is simply predisposed to damage by alkalies. If the noxa is allowed to act intensively necrosis occurs, but if it only barely exceeds the threshold of tolerance then a non-specific dermatitis develops; clinically this is often indistinguishable from allergic contact eczema. But we know from clinical observation and experimental work that this toxic damage predisposes to allergic sensitivity to the noxa itself or to other contactants encountered at the same time. Many occupational eczemas begin as a toxic injury (primary irritant dermatitis) which is often conditioned by a diminished power of resistance; hence the study of cutaneous resistance to certain harmful substances is of significance in the pathogenesis of eczema

In practice alkaline noxae such as soap soda lye, cement and lime play the biggest part, hence the skin's resistance to alkalies and its ability to neutralize them are of prime importance and have been investigated most frequently Recently similar studies have been carried out with regard to acids. The important practical problem of vulnerability to commercial solvents has been comparatively little examined, and thorough studies of cutaneous resistance to other noxae have not been published

CUTANEOUS NEUTRALIZATION OF, AND RESISTANCE TO ALKALIES

In 1935 I described a simple method of determining the alkali *neutralizing power* of the skin —

TECHNIQUE. Equipment consists of two pipettes which deliver 28 to 34 drops of water per ml a freshly prepared solution of N/80 NaOH a 0·05 per cent. solution of phenolphthalein in alcohol, ten glass or plexiglass blocks (3 5 by 2 cm base 1 5 cm. height) skin pencil, stop watch and cotton wool

The test is made on healthy skin preferably on the extensor surface of the forearm, lateral side of arm, the back or the upper anterior surface of the leg The area to be tested is outlined with the skin pencil in the dimensions of a glass block One drop each of the N/80 NaOH and indicator solution are let fall in this area and covered with a glass block *The time required for decolorization is now measured with the* stop watch. The glass block is rocked every 30 seconds to ensure proper mixing of the solutions. Phenolphthalein becomes colourless at *p*H 8 3 and several minutes elapse before this occurs. The glass block is then removed, the skin cleaned with cotton wool, a fresh drop of each solution applied and a clean glass block used as a cover This procedure is repeated on the same area ten times in all each test being timed as before Results are entered as follows

Type A	Rapid Neutralization	None of the ten estimations exceed 5 minutes.
Type B	Medium Neutralization	One or more estimations lie between 5 and 7 minutes, but none exceed 7 minutes
Type C	Slow Neutralization	One or more estimations exceed 7 minutes.

In addition to this method I described[3] a means of testing the skin's *resistance* to stronger lyes, using the onset of visible cutaneous damage as the indicator

TECHNIQUE three neighbouring areas of the dimensions of a glass block are outlined on the selected site Each area is moistened with a drop of N/2 NaOH and covered with a glass block these are removed after ten minutes and the fields examined for evidence of skin damage *in the shape of small papules or vesicles.* After wiping with cotton wool one area is left untouched and Nos. 2 and 3 treated as before and re examined after ten minutes Finally only area No 3 is treated Reactions often appear *only ten to twenty minutes after the test* only distinct papules and vesicles, not simple erythema are regarded as showing a positive result. Readings should be repeated after twenty four hours when the punctate sites of alkali damage appear as tiny crusts.

Subjects with a diminished resistance to alkalies react to one or two ten minute applications a reaction to three applications is normal but may be lacking in persons with an increased resistance

Other methods which have been used include the following: Koch tested the alkali-neutralization of the skin by measuring the shift in pH of a caustic soda solution with the quinhydrone electrode. Vermeer[1] applies solutions of N/40, N/20 and N/10 NaOH and covers them with cellophane, estimating the time needed to decolourize the phenolphthalein indicator. In normal subjects the times stand in a ratio of 1 2 4 whereas in those with a diminished resistance to alkalies they are as 1 2 1. As we shall see later this rapid neutralization of N/10 NaOH follows breaching of the stratum corneum with diffusion of tissue fluid. I have in the past tested alkali-resistance with patch tests of graduated concentrations of lime water. Similarly one can use varying strengths of soft soap or sodium oleate as patch tests.

Measuring the actual pH of the skin represents a complete chapter in cutaneous physiology and a series of publications have appeared recently. This estimation informs us only of the state of affairs at the moment of testing and gives relatively little information regarding alkali reserve, neutralizing power and resistance. One can, however, determine the time which elapses before the pH returns to normal after exposure to alkalies.

RESULTS. The alkali neutralization test with N/80 NaOH was performed at my Institute in 618 healthy controls and 195 eczema patients; the histories of the latter gave evidence of damage from alkaline noxae. The results, along with those of other authors[4] are presented in Table IV.

Persons with delayed alkali-neutralization seem to be particularly susceptible to eczema from alkalies; they probably originate in the first instance from the 14-19 per cent. of the population which has a diminished resistance. Nevertheless, such a delayed capacity to neutralize alkalies is not an absolute condition for the development of alkali damage or eczema, in view of our finding good neutralizing capacity in 10 per cent. of cases of cement and soap eczema.

The high incidence of subjects with poor alkali neutralizing powers is less pronounced in other aetiological groups, such as the seborrhoeic and endogenous, and contact eczema from non-alkaline noxae.

With regard to alkali-resistance against N/2 NaOH tests were made in 422 controls and 129 cases of alkali eczema. Among the former 85 per cent. showed good resistance, among the latter only 30 per cent. This direct method therefore confirms the fact that patients with alkali eczema with a few exceptions, show a diminished resistance to lyes.

These technical details are given in full, as likely to be of practical assistance, for instance in the selection of industrial workers. *Ed.*

Both methods of examination were used in most of the subjects. On the whole good alkali neutralization accompanied good resistance, and *vice versa* but we saw a *few exceptions to this rule, in* that poor resistance could be associated with good neutralizing

TABLE IV

ALKALI NEUTRALIZATION TEST

AUTHOR	METHOD	NUMBER OF CASES	A RAPID	B MEDIUM	C SLOW
		(a) In Controls			
Burckhardt and co-worker	N/80 NaOH	618	67%	19%	14
Zingsheim, Franken, Schmid, *Heinz, Stopanski*	N/80 NaOH	559	63%	18%	19
Vermeer	1/40 1/20, *1/10 NaOH*	70	64%	18%	18
Koch	Electrometric	63	13%	60%	7
		(b) In Alkali Eczema			
Burckhardt and co-worker	N/80 NaOH.	195	16%	19	71%
Zingsheim, Franken, Schmid, *Heinz, Stopanski*	N/80 NaOH	107	7	6%	67%
Vermeer	1/40 1/20, 1/10 NaOH.	19	11%	31	58
Koch	Electrometric.	15	0%	0	100
		(c) In Seborrhoeic and Endogenous Eczemas			
Burckhardt, Franken Zingsheim, Schmid.	N/80 NaOH.	141	34%	40	6

capacity With a thin stratum corneum the possibility exists that even N/80 NaOH can cause damage and penetration into the deeper layers of the epidermis and consequent rapid neutralization by tissue fluids.

PHYSIOLOGICAL BASIS OF ALKALI NEUTRALIZATION

The following are the operative factors in alkali neutralization the stratum corneum with its proteins, the sebum the sweat carbon

dioxide and, after a breach of the stratum corneum has occurred, the tissue fluids.

Rôle of the Stratum Corneum and its Proteins. Areas with a thickened horny layer such as the palms and soles, show an increased alkali resistance and an accelerated alkali neutralization. According to Miescher[33] repeated irradiation with natural or artificial sunlight leads to thickening of the stratum corneum and skin thus treated also shows accelerated neutralization and improved resistance. The opposite is seen in persons with a disease of the horny layer such as ichthyosis. Patients with alkali eczema show less marked differences in neutralization and resistance between areas where the horny layer is thicker or thinner in such subjects a thickening of the stratum corneum does not produce the same beneficial effects as in normal persons This suggests that the quality of the horny layer may be of importance, and not only its thickness. One may infer that patients suffering from alkali eczema have a stratum corneum of inferior quality Jacobi s investigations make it seem probable that the amino-acids of the stratum corneum neutralize alkalies; similarly Vermeer[4] and Rothman and their co-workers have shown that the skin produces amino-acids which act as amphoteric substances in combining with acids and alkalies. According to Vermeer the thickened horny layer produced by ultra violet irradiation delivered persistently higher amounts of amino-acids. Spier and Natzel[38] found a correlation between efficient alkali neutralization and protein production.

Rôle of Sebum. Alkali neutralization and resistance are usually diminished in skin which has been de-fatted with ether Infants and children, whose skin produces little sebum, show poor alkali resistance and neutralization. As sebum itself possesses little neutralizing power its action is attributed to a colloid-chemical mechanism. Clinical experience shows that a combination of de greasing and alkaline agents can damage the skin severely thus we have seen cutaneous damage following the successive effects of organic solvents, such as benzine, benzol or aliphatic sulphonic esters, and alkalies.

Rôle of Sweat. Both alkali neutralization and resistance are improved during sweating produced by pilocarpine[3] or the carbon-arc lamp[5] injection of atropine has the opposite effect. Certain eczema patients produce highly alkaline sweat during acute exacer bations; this temporarily increases the pH of the skin and impairs alkali resistance and neutralization. Sweat probably contributes to

neutralization in different ways in the normal skin however when sweating is not taking place, it probably plays a minor part, as evidenced by the efficient neutralization which can occur along with impaired sweat secretion

Rôle of Carbonic Acid. Diffusion of carbonic acid takes place from within it is most marked where the stratum corneum is thin, and least where it is thick. When the skin has been damaged by strong alkalies carbonic acid diffusion increases.[11] Where the skin is intact, however it is unlikely that carbonic acid plays any significant part in alkali neutralization or resistance. When resistance is low however even dilute lyes, such as N/10 NaOH can cause damage, and it is in these circumstances that carbonic acid and tissue juices act as neutralizers. Vermeer s method outlined above, depends on this phenomenon

Is the Capacity to Neutralize Alkalies a Constant Individual Property?

Reference has been made to a lower alkali resistance and neutralizing power in childhood similarly Savary[11] found a slight diminution between the ages of sixty-five and ninety two attributable to senile atrophy Apart from the age factor the cutaneous capacity to neutralize alkalies seems to be an individual attribute. Thus on re-examining sixty-eight patients with lowered alkali neutralizing capacity after two to twelve years we found no change in fifty improvement by one grade (e.g Type C to Type B) in fifteen and by two grades in three. Schmid likewise found no improvement in alkali neutralization after healing of the eczema Meyer and Economopoulos, on the other hand noted a return to normal in the course of healing but according to Wacek this is the exception and not the rule. In testing forty-eight cases of eczema alkali resistance was improved on recovery in only five, neutralization in eight. Apart from variations due to age, alkali resistance seems to be an individual constant property subject only to secondary fluctuations by seasonal changes in the thickness of the stratum corneum and periodic alterations in sweating

The Significance of Alkali Damage and Alkali Resistance of the Skin in the Pathogenesis of Eczema

I have only rarely seen an allergic hypersensitivity to chemically pure alkalies such as sodium or calcium hydroxide In cases of so-called alkali eczema it is usual to find allergic sensitivity to

several other occupational contactants. In housewives and painters this is commonly a sensitivity to turpentine in doctors and dentists to drugs, local anaesthetics and antiseptics; in bricklayers and washerwomen to potassium bichromate, which may be present in cement and eau de javelle[44, 45]; in hairdressers to dyes or thioglycolate, a constituent of the cold wave process; in nickel platers to the metal itself. In all these occupations frequent contact with alkalies facilitates subsequent sensitization, and I have been able to demonstrate this experimentally in humans and guinea-pigs.[78] In one series of eight subjects two were found to react to an application of nickel sulphate solution; in a second series of seven, in whom the skin was first prepared with soft soap or lime water six showed a sensitivity reaction. This was particularly marked in four women with reduced alkali resistance, in whom the soft soap had produced greater damage. Haxthausen[79] was also able to produce a high degree of sensitivity to nickel and cobalt in this way. In guinea pig experiments the combination of alkali damage and antigen application also produced more frequent and rapid sensitization than the application of antigen alone.

Healthy skin can neutralize alkalies up to a certain point, hence washing with soaps of low alkali reserve is tolerated. Frequent washing with strongly alkaline products, or contact with lime or cement, can damage the skin and facilitate sensitization; this applies even to persons who possess a good alkali resistance and *a fortiori* to those who do not. In Zürich I have started to test candidates for technical schools with regard to their alkali resistance and advise young people with deficient resistance to avoid such occupations as bricklaying, hairdressing and painting.

These tests are also applicable to diagnosis in that they may draw attention to alkaline noxae in cases of occupational eczema.

CUTANEOUS NEUTRALIZATION OF AND RESISTANCE TO ACIDS

The acid resistance of the skin may be estimated by patch tests with graduated dilutions of hydrochloric acid, a positive reaction appearing as papules and pustules. Table V is compiled from Miescher's[76] and Burckhardt and Baumle's[31] figures.

Thus the skin tolerates fairly high concentrations of hydrochloric acid and for this reason Mentschel[77] speaks of the skin's acid resistance, in contrast to its alkali sensitivity. For testing acid

neutralization in different ways in the normal skin however when sweating is not taking place, it probably plays a minor part, as evidenced by the efficient neutralization which can occur along with impaired sweat secretion

Rôle of Carbonic Acid. Diffusion of carbonic acid takes place from within It is most marked *where the stratum corneum is thin*, and least where it is thick When the skin has been damaged by strong alkalies carbonic acid diffusion increases.[**, 1] Where the skin is intact, however it is *unlikely that carbonic acid plays any* significant part in alkali neutralization or resistance. When resistance is low however even dilute lyes, such as N/10 NaOH can cause damage, and it is in these circumstances that carbonic acid and tissue juices act as neutralizers. Vermeer s method outlined above depends on this phenomenon.

Is the Capacity to Neutralize Alkalies a Constant Individual Property?

Reference has been made to a lower alkali resistance and neutralizing power in childhood, similarly Savary[**] found a slight diminution between the ages of sixty-five and ninety-two attributable to senile atrophy Apart from the age factor the cutaneous capacity to neutralize alkalies seems to be an individual attribute. Thus, on re-examining sixty-eight patients with lowered alkali neutralizing capacity after two to twelve years we found no change in fifty improvement by one grade (*e.g Type C to Type B*) in fifteen and by two grades in three. *Schmid likewise found no improvement* in alkali neutralization after healing of the eczema. Meyer and Economopoulos, on the other hand noted a return to normal in the course of healing but according to Wacek this is the exception and not the rule. In testing forty-eight cases of eczema alkali resistance was improved on recovery in only five, neutralization in eight. Apart from variations due to age, alkali resistance seems to be an individual constant property subject only to secondary fluctuations by seasonal changes in the thickness of the *stratum* corneum and periodic alterations in sweating

The Significance of Alkali Damage and Alkali Resistance of the Skin in the Pathogenesis of Eczema

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P W Schmidt[34] tested acid neutralization of hydrochloric acid with the quinhydrone electrode. Jacobi[35] used methyl orange as indicator with a method similar to Burckhardt's technique for alkali neutralization.

Acid resistance may play a decisive rôle in occupational dermatoses from acids. P W Schmidt frequently found delay in HCl neutralization in cases of baker's eczema, while Heinz, in the same type of case, found delayed alkali neutralization. It is therefore probable that a diminished buffer capacity of the stratum corneum is of significance in cases of damage from acids as well as alkalies.

RESISTANCE OF THE SKIN TO COMMERCIAL SOLVENTS

Organic solvents such as benzine, benzol, xylol and toluol are extensively used in industry and not infrequently give rise to dermatitis. Sensitization to these substances is seen only rarely whereas it is commonly observed with turpentine, which is widely used as a solvent.

INVESTIGATIONAL METHODS. Mayer[44] and Hoffmann[37] employed patch tests, using concentrations of 50-90 per cent. in olive oil. The same procedure was used by Burckhardt and Danbolt[38] in testing resistance to turpentine As the majority of these substances are volatile methods have been elaborated whereby the solvent is brought in contact with the skin in a sealed chamber Prowig[39] and Leder[40] used small glass cylinders of 22 mm. diameter closed at the top with a tap and kept in contact with the forearm by rubber bands, each cylinder contains a column of the test fluid 10 mm. high. For determining the resistance graduated times of contact are used, the various cylinders remaining on the skin for periods of five, ten, fifteen, twenty twenty-five or thirty minutes. In addition to an early reaction, characterized by redness and burning after three to nineteen minutes, a late reaction, which reaches its maximum in from two to four days, is also seen. Changes from erythema to vesiculation are produced, depending on the degree of damage.

RESULTS Danbolt and Burckhardt found that 94 out of 166 subjects with healthy skins showed a toxic reaction to undiluted oil of turpentine. This toxic reaction consists of a sharply circumscribed, superficial necrosis which is to be distinguished from an allergic eczematous reaction. A half of the subjects showed a toxic reaction with a 30 per cent. solution, and a 10 per cent. solution was tolerated by all. Turpentine is not a simple chemical substance and its toxicity and sensitizing properties depend on its content of oxidized compounds (Burckhardt and Schaaf Hellerström[41])

TABLE V

THRESHOLD OF REACTION TO VARIOUS CONCENTRATIONS OF HYDROCHLORIC ACID

Percentage of HCl Solution	*Percentage of subjects showing threshold of reaction*
4	4 5
6	4 5
8	47 0
1	_5·0
18	19 0

neutralization Schuppli[13] has devised a method which has also been used by Burckhardt and Bäumle, Schmid and Wacek.[8]

TECHNIQUE. Solutions of HCl, of strengths varying from 0·05 to 1 5 per cent., contain 1 ml. of 0·3 per cent. bromphenolblue solution in each 5 ml One drop of each dilution (concentrations 0·05 0 075 0·1 0·15 then by increments of 0·05) is placed in series on the arm and spread with a glass block as in the alkali neutralization test. The colour changes from yellow to blue at between pH 2 8 and 4·6 the application showing the earliest colour change is noted after one minute Recognition of this threshold is difficult and consequently different workers have found different results the averages for normal persons have been given by the authors quoted as 0·45 per cent., 0·15 per cent., 0·4 per cent and 0·25 per cent. The relative values are therefore of more interest than the absolute.

According to Burckhardt and Bäumle subjects with a high acid resistance threshold show good acid neutralization, and *vice versa* Neutralization is better on areas where the stratum corneum is thick and also during sweating produced by pilocarpine or the carbon arc lamp atropine has the opposite effect. In this respect there is a parallel relationship with alkali neutralization and it is therefore probable that both phenomena depend on the same factors which like the proteins of the horny layer have amphoteric properties.

Both in healthy individuals and in patients with chronic or healed eczema one often finds a parallel slowing of alkali and acid neutralization In acute eczema acid neutralization is sometimes improved, becoming normal during the course of the disease. According to Schmid s investigations this probably results from the secretion of a strongly alkaline sweat during the acute phase

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Diminished resistance predisposes not only to toxic damage, but also to sensitization since these properties are linked

Thresholds of reaction to benzol benzine, *xylol toluol* and petroleum ether (solvent naphtha) lie between 70 and 85 per cent, according to Mayer and Hoffmann and are reduced to 50 to 70 per cent in persons with eczema from organic solvents Resistance to the various solvents usually runs parallel but the less volatile substances were more toxic Pröwig and Leder tested resistance to hexane and benzine in 208 subjects (*see* Table VI)

TABLE VI

THRESHOLD OF REACTION TO HEXANE AND BENZINE IN 208 SUBJECTS

Time in minutes required for reaction to appear	*Percentage of Subjects reacting*
5	
10	20
15	45
20	20
25	10
30	3

Before puberty 85 per cent. show a threshold of fifteen minutes. Individual variations probably depend partly on different amounts of sebum which is deficient before puberty Areas with a thickened stratum corneum show a higher resistance, while local anaemia produced by adrenaline iontophoresis produces a diminution *Organic solvents are absorbed by the skin* ; *if their removal by* the blood stream is hindered they accumulate in the skin and cause more damage Pröwig and Leder did not find a diminution of benzine resistance in ninety-five cases of eczema of various causation and only once in seven cases of eczema caused by organic solvents

A reduced resistance to solvents is a decisive factor in toxic damage and sensitization from turpentine; it also seems to be more frequent where benzol xylol and toluol have caused toxic damage in the case of benzine the significance of lessened resistance has not yet been clarified

CONCLUSIONS

We have seen that many data have been collected in connection with the skin's capacity to resist and neutralize alkalies, and that we also possess some knowledge of acid neutralization and resistance to organic solvents. The skin's protective function in respect of these different substances depends largely on the same factors. The stratum corneum is of importance in the first line of defence; hence areas where it is thick have a higher resistance to alkalies, acids and solvents, while resistance is less where it is thin or where it has been damaged. The sebum forms a physical-chemical barrier and is of importance in all cases. The secretion of sweat, with its changing concentration and constitution, affects the neutralization of acids and lyes, while the universally diffused carbonic acid plays only a fortuitous and subsidiary part in the resistance of intact skin

The quality of the stratum corneum is probably a highly individual property and determines the individual factor in resistance. Thorough study of its chemistry particularly of its proteins, may in the future throw more light on this individual factor

Clinical observations and experimental work indicate that toxic damage to the skin, especially by alkalies, causes not only non-specific dermatitis but facilitates the development of allergic contact eczema. It follows that, in order to prevent eczema, toxic damage, particularly by alkalies, must be avoided. As people with diminished resistance are particularly endangered they should be subjected to the minimum possible exposure to these noxae.

*

EDITOR'S NOTE

At this juncture it seems appropriate to refer to certain further implications of alkali neutralization capacity The next chapter deals with the part played by bacteria in producing or maintaining eczemas of various kinds; it is therefore reasonable to speculate on the factors which promote or discourage the growth of surface bacteria Burtenshaw[4] has summarized a quantity of his own and others work on the self-sterilizing power of the skin: the pH of the skin surface is one of the most important factors affecting the growth of surface organisms. *In vivo* as *in vitro* these are adversely affected by a fall in pH, values of 5 0 or less are considered normal for the dry skin surface and it is at pH 5 0 and below that the

organisms in question show a decisive inhibition of growth Marchionini s work[44] purported to map out areas of relative alkalinity or as he termed it, gaps in the acid mantle of the skin." It is interesting to note that these areas are predominantly involved in acute bacterial eczema of the type described as producing an exuberant growth of staphylococci (Chapter VII) Many dermatologists still prefer to attach the label "seborrhoeic" to this clinical type.

It seems possible then that the work outlined in this chapter may have a direct bearing on the subject of the next. Burckhardt states that the incidence of defective alkali neutralization was not so marked in subjects of seborrhoeic eczema as in those whose eczema was directly attributable to alkaline noxae; nevertheless he shows that some deviation from normal values did exist. It is thus possible that an inherent defect in alkali neutralizing capacity may be one of the predisposing causes of bacterial as well as of alkali and contact eczemas.

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CHAPTER VII

THE ROLE OF BACTERIA IN ECZEMA

H STORCK

I INTRODUCTION

ECZEMAS of widely differing morphology localization and distribution do not by any means invariably admit of aetiological solution by patch tests with external contactants, even after careful history taking. Even when the initiating contact allergy has been discovered with certainty the mechanism of chronicity dissemination in successive crops and rhythmical recurrences *in spite of exclusion of the offending contactant* remains a riddle

It is important to know therefore to what extent unexplained eczemas and contact eczema with subsequent complications may be explained by a cutaneous reaction to microbes resident on the skin surface or in internal foci and consequently amenable to specific anti-bacterial treatment

The proposition originally put forward by Unna in 1896 that eczemas are always microbial being caused by infection with the "morococcus" was untenable since it was shown by Kreibich Neisser Scholtz, Jadassohn Török Brocq Veillon and others (under Ref 2) that the primary eczema vesicle is sterile One could then, at the most, assume an allergic reaction to bacterial products. Following this, the most diverse bacteria obviously unrelated to morococci, were incriminated with more or less justification. But conclusive *functional* skin tests were carried out only sporadically before 1930 positive results being reported by Scholtz and Raab Bender Bockhart and Gerlach Azua and Mendoza Rajka and Peter[2] The French school under Sabouraud s leadership used painstaking *cultural and histological methods to demonstrate* streptococci staphylococci and occasionally yeasts in fresh lesions of eczema their aetiological significance was inferred rather from their mere presence and *ex juvantibus* than from cutaneous tests.

The significance of a microbial cause in certain types of eczema was expressed by such terms as "*Streptococcides et staphylococcides eczématiformes*" (Sabouraud) and "*dermo-épidermite microbielle*" (Gougerot).

At Miescher's instigation, Robert, working at the Dermatological Clinic of Zürich, performed patch tests with filtrates from cultures of cutaneous organisms; this allowed of an exact evaluation of the significance of bacteria in the genesis of eczema, on a sound functional basis. *Filtrates of broth cultures of Staphylococcus aureus provoked eczematoid reactions* with typical spongiosis histologically with especial frequency; this was observed chiefly in eczema patients, less often in normal persons. That the nature of these reactions was allergic and not toxic, was inferred from their lack of correlation with the antihaemolysin titre. Later Storck[4] was able to show that in occasional cases true eczematous patch test reactions could be obtained with organisms cultured from eczema lesions and that in various types of eczema cutaneous microbes were of major importance or of exclusive significance. Rajka, using the indirect passive transfer method in man, was able to demonstrate specific, mobile, bacterial reagins, and in a few cases positive blood cultures were obtained at the beginning of dissemination of an eczema. Finally Hellesen showed that the specific manner in which the skin reacts *in vivo* to certain bacterial strains could be paralleled *in vitro* by agglutination reactions and phage-typing.

2. THE BACTERIAL FLORA OF NORMAL AND ECZEMATOUS SKINS

A qualitative and quantitative knowledge of the bacteria resident on healthy and eczematous skin is of first importance in assessing the significance of bacteria in eczema.

Qualitatively there is scarcely any difference between the flora of healthy and eczematous skin, in the former besides the common saprophytic cocci, *Streptococcus haemolyticus* is found in 7.5 to 56 per cent. according to the technique of culture inoculation, and *Staphylococcus aureus* in 0 to 62 per cent. From eczema lesions, in addition to saprophytic cocci, *Streptococcus haemolyticus* is recovered in up to 50 per cent. and *Staphylococcus aureus* in 58 to 100 per cent. (Rajka, Feigina and Lourjé—100 per cent., Feldman and Mimaker—76 per cent. Edel—97 per cent., Davies, Nixon *et al.*—92 per cent.[9]) Table VII lists the organisms isolated

from the eczematous lesions of *110* patients, not only with regard to their relative frequency but also with regard to their skin reactivity as measured by the results of epicutaneous patch tests. It is seen that *Staphylococcus aureus* and *Streptococcus haemolyticus* are both frequent and skin reactive, which agrees with the results of Robert, Rajka Heilesen Ulbricht, and others.

TABLE VII

BACTERIAL FLORA FROM THE ECZEMATOUS SKIN OF 110 PATIENTS. RESULTS OF EPICUTANEOUS PATCH TESTS WITH THESE ORGANISMS

Type of Bacteria	Number of times found	Percentage	Number of cases with marked 4 hour reaction
Staphylococcus aureus	101	9	69 (65%)
Sarcina	60	55	—
Dissociated Staphylococci	54	49	—
Diphtheroids	5	47	—
Enterococcus	45	41	(4%)
Streptococcus haemolyticus	41	37	10 (?4%)
Streptococcus non-haemolyticus	34	31	—
Gram negative bacilli (Flavo, Heringslake, etc.)	33	30	—
Staph albus	31	29	(6)
Saprococci	5	3	—
E. coli	18	16	(18%)
Ps. pyocyanea	8	7	—
Mesentericus, Mycoides	6	5	
Proteus vulgaris	5	4 5	—
Staph. citreus	4	4	—
Anaerobic gram positive bacilli	4	4	
Ps. fluorescens			—
Candida albicans	1	1	—

But if there is little difference qualitatively between the organisms on healthy and eczematous skin there is a marked contrast

quantitatively Cultures produced by pressing plates of solid media against the skin surface* result in densely aggregated colonies of *Staphylococcus aureus* when taken from the following types of lesions:

Acute, infiltrated, erythemato-squamous† more or less sharply circumscribed mycosiform (*i.e.* resembling tinea corporis) with predilection for the flexures† lesions situated on the lower leg (Eczema rubrum) psoriasiform and lichenified eczema particularly erythemato-vesicular and weeping areas.

The staphylococci grown from these types of lesion are particularly active in patch tests.

Staphylococci are not increased in the following types of lesion:

(1) dry erythemato-squamous seborrhoeic areas;

(2) erythemato-papular and pityriasiform areas of dissemination.

No marked differences are seen between the numbers of streptococci gram-negative bacilli and common saprophytic cocci on normal and eczematous skin. Apart from the strains which can also be recovered from normal skin no special organisms can be recovered from areas of eczema, that is no organisms which could be regarded as specific agents in the production of eczema, as postulated by Unna.

The epicutaneous patch test may be regarded as an adequate, functional skin test. Hence this test is decisive in determining the aetiological significance, not only of simple chemical substances, but also of microbes; it has recently been more generally employed, using live broth cultures filtrates and killed bacteria. In order to facilitate the action on the epidermis of the relatively large molecules of the bacterial products, the surface of the skin can be lightly excoriated with powdered glass wool.

The twenty-four hour positive patch test results shown in Table VII are clinically visible as small erythemato-papular areas of eczema (Figs. 41 42) sometimes with vesicles and weeping points, more rarely with pustules. *Histologically* they show circumscribed spongiosis with lymphocyte immigration, as in positive patch test results with simple chemicals (Fig. 44). In contrast, however and particularly after preliminary excoriation with glass wool there may be necrobiotic changes with impaired staining of nuclei, as well as oedematous spongiosis; this results in an area of poorly

* The author refers to this method as *Abklatsch*; it will later be termed "contact culture" *Ed.*

† These forms are sometimes referred to as "seborrhoeic." *Ed.*

stained swollen cells connected by broad processes to form a clumsy network (Miescher[a]). Polymorphs often predominate in the infiltrate.



A



Fig. 40A.—Exudative seborrhoeic (bacterial) eczema.
Fig. 40B.—Contact culture plate almost overgrown with *Staphylococcus aureus* and a fair number of *Streptococcus haemolyticus*. Taken from eczematous area, right ear.
Fig. 40C.—Sparse colonies of various organisms from healthy skin of arm of same patient.

Positive patch tests made with broth cultures and filtrates of *Staphylococcus aureus* and *Streptococcus haemolyticus* as well as other bacteria are found more frequently in eczema cases than in

controls; the comparative figures for *S. aureus* are 56 per cent. against 33 per cent. for *S. haemolyticus* 20 per cent. against 5 per cent. Strongly positive reactions are particularly frequent in patients



FIG. 41A.—Localised eczematous area of breast.
FIG. 41 [illegible]—Result of patch test to autogenous culture of *Staphylococcus* [illegible] and to mixed culture.
FIG. 41C.—Contact culture from lesion shown in A.
FIG. 41 [illegible]—Contact culture from normal skin of same patient.

with the types of lesion that produce exuberant contact cultures. Figures 40, 41 and 42 show examples of bacterial eczema. In Figures 40 and 41 are shown the demonstrably more profuse growth, chiefly of *S. aureus*, from eczematous as compared with normal skin areas, by contact culture. Figures 41 and 42 also show the marked



FIG. 4 A.—Localized eczematous areas on backs of hands.
FIG. 42B.—Result of patch tests to broth filtrates of *Staphylococcus aureus* (A), *F . . . rococcus* (E) and control with broth only (K).

positive reactions of patch tests performed with bacteria cultured from the affected areas. Bacterial eczema can be grafted on to a dry seborrhoeic eczema, as in Figure 40A, or it can be produced by



FIG. 43.—Pityriasiform eczema.
FIG. 43B.—Contact culture from healthy skin.
FIG. 43C.—Contact culture from affected area.
Note that there is no increase of organisms in the culture from this type of eczematous lesion.

constant scratching, for instance with scabies, as in Figure 41 or it can appear without external cause and in the absence of a pre-existing dermatosis, as in Figure 42. Similar primary and secondary

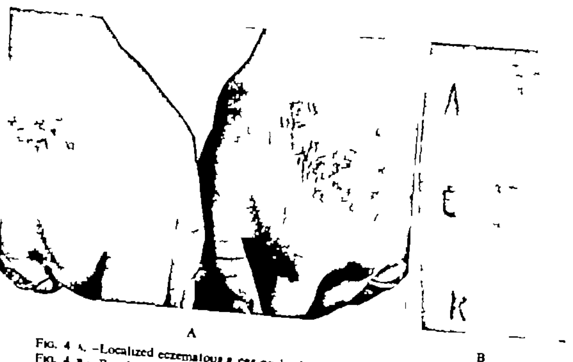


FIG. 4 A.—Localized eczematous a eas on backs of hands.
FIG. 4 B.—Result of patch tests to broth filtrates of *Staphylococcu au eu* (A), *Ent rococcu* (E) and cont ol with broth o ly (K).

eczema exacerbation of the primary focus was seen in sixteen after vaccine injection, occasionally with the phenomenon of dissemination; in a few instances generalized pruritus, fever urticaria and joint swellings also appeared

In animal experiments it has been possible to produce an eczematous sensitivity to cutaneous *staphylococci* and their filtrates; this was achieved by repeated inunction of broth cultures or filtrates. The eczematoid reaction is seen not only macroscopically but histologically as spongiosis with lymphocytic infiltration



FIG. 44
Localized spongiosis and vesiculation after 24 hours patch testing with broth filtrate of *Staphylococcus aureus*.

oedematous necrosis, and occasional increase of granulocytes. The reaction can also be elicited by intracerebral injections of small quantities of bacterial filtrate.

4. NATURE OF THE ALLERGEN IN BACTERIAL ECZEMA

In considering the rôle of bacteria in the local spread chronicity and dissemination of eczema we must take into account, not only the results of contact cultures and patch tests, but the empirical, generally accepted recognition of the eczematogenous action of bacteria. In addition, a simple, localized contact eczema may undoubtedly be secondarily infected and produce a generalized eczema after a certain time has elapsed for sensitization to develop

It is not clear to what extent these phenomena depend on bacterial action. Possibly alterations in sensitivity or immunity to bacteria and their products, or even to complex allergens elaborated by them play a decisive part. Rajka who isolated pyococci from

bacterial eczemas can be demonstrated by contact culture and patch tests after injury (paratraumatic) pyodermas, fissures, and contact eczemas of widely different localization and distribution Clinically the eczematous areas are almost always acutely inflamed, vesicular and crusted or of the squamous seborrhoeic type. Dry slightly infiltrated mycosiform areas or generalized pityriasiform areas of dissemination generally show no qualitative or quantitative difference from normal in their bacterial flora the results of skin tests are also rarely positive (Fig. 43)

Patch tests usually show reactions of equal intensity with broth cultures and bacterial filtrates though occasionally one sees cases where either gives a stronger reaction than the other Killed washed bacteria usually give only weak reactions.

As great numbers of bacteria with cutaneous activity do actually occur at least in the primary lesions then the question arises as to whether and in what way allergens elaborated at the primary focus can produce or maintain progressive eczema and distant eczematoid bacterids.

3. EXPERIMENTAL PROVOCATION OF ECZEMA BY BACTERIA OR THEIR PRODUCTS

It is extremely difficult to produce progressing bacterial eczemas in sensitized individuals by inoculation of living cultures of surface bacteria this can be achieved only when an extremely active strain is used in a highly sensitive subject Occasionally it can be brought about by repeated daily inunction of the appropriate strain more commonly it can be produced by a twenty four-hour compress of living broth culture on healthy skin and still more easily by re inoculation of healed areas of eczema this last may succeed in exacerbating the eczema and producing dissemination Yet the sensitivity to the epicutaneous application of bacteria does not seem to be particularly great, as exacerbation of a primary eczematous focus by such tests is seen only rarely while crops of disseminated eczema practically never occur this is in contrast to their occasional appearance in hypersensitive patients after application of patch tests with the specific relatively simple chemical contactant Exacerbation of the primary focus is seen more commonly after intracutaneous or subcutaneous injection of autogenous or mixed vaccine and occasionally even pityriasiform or papulo-vesicular areas of dissemination, or a scarlatiniform exanthem appear (Robert Rajka) In sixty nine personally observed cases of chronic recurrent

It should be noted that there is no negative correlation either as diminution of antitoxin is not a constant finding in cases with positive cutaneous reactions (Robert, Storck[*])

Specificity As is the case with allergic reactions, so the eczematous response to cutaneous bacteria is strongly specific: individual patients react only to individual strains. Thus there are strains of staphylococci which produce marked reactions in only a few sensitized persons, and not in others; again, one finds strains which cause reactions in a large percentage of cases. Similarly one sees patients who react to a wide selection of strains, and others who react slightly or not at all. Corresponding to these specific *in vitro* allergenic variations, strains which produce eczema have been separated and established *in vitro* by the agglutination method and by phage typing (Heilesen) *It has been shown that the same strains of bacteria occur both on the skin and in the naso-pharynx* The eczema-producing strains differ serologically from the pathogenic strains, and this is in agreement with the observation that impetig inization and furuncles practically never occur after patch testing with live cultures of the former type.

Though bacteria and their filtrates produce markedly positive eczematous patch test reactions, such results differ *in degree* from the natural conditions obtaining with acute weeping exacerbations. Yet our artificial methods bring either living cultures in contact with the skin in a moist chamber for periods of twenty-four hours, or filtrates which are the result of ten to fourteen days incubation. *Thus these fairly* concentrated bacterial products, kept in contact with the skin for relatively long periods, seem to react mildly by comparison with the natural conditions mentioned above. One must therefore think of the possibility that bacteria may under natural conditions, elaborate complex allergens which can only be obtained with difficulty *in vitro* *So far the* demonstration of such complex allergens in man or experimental animals has not been made with certainty Rajka, however believed that incubation of staphylococci with vesicle contents intensified the intracutaneous reaction. Robert, on the other hand, was unable to produce stronger reactions to bacterial filtrates after their incubation with sweat or skin extract, and we have had similar negative results in animal experiments, using bacteria or their filtrates after incubation with macerated or minced skin.

Recent work on autosensitization (see Chapters III and IX) whereby the combination of bacterial products and organ extracts

blood cultures in ten out of forty-two cases at the time of dissemination of an eczema showed that bacteria can be of significance during this phase. The fact that different types of eczema may disseminate, usually in a similar symmetrical manner and affect the face and neck, then the trunk and limbs, with predilection for the flexures (Miescher Zuber[4]) suggests a similar pathogenetic mechanism It is not yet clear whether this phenomenon is predominantly a microbial effect, or due to other mechanisms.*

Chemical research has shown that the eczematogenic agent in bacteria is of a protein nature (Miescher Lincke & Storck[10]) We are thus dealing with relatively large protein molecules, which can themselves act as antigens without the necessity of acquiring a protein linkage, as is the case with the relatively simple chemical antigens

This eczematogenic function of proteins shows the close relationship between bacterial eczema and the allergy of infection. In both forms, as well as in simple contact eczema, the antibodies seem to be sessile and passive transfer is successful only by transfer of sensitized cells. The reaction is independent of the blood vessels, and its chief characteristic is the *delayed reaction* in contrast to the *immediate* anaphylactic reaction (Rich, Raffel [3]) It is interesting to note that, according to Raffel a waxy lipid fraction of the infecting organism is responsible for the delayed reaction in the allergy of infection After addition of this fraction to the protein antigens which produce an anaphylactic reaction, this immediate reaction can be changed to a delayed reaction. *It* is possible that, in the delayed type of reaction seen in eczema, lipid *fractions derived from the epidermis may be concerned* and in the case of bacterial eczema lipid fractions derived from the organisms

But despite a relationship with the allergy of infection there seems to be a specific epidermal factor in bacterial eczema. Neither in man nor in experimental animals do the courses of epicutaneous and intra*cutaneous reactions run parallel further in animals epidermal sensitivity* may be induced by repeated inunction of sterile filtrates, in contrast to the allergy of infection where only living or dead organisms can act as antigens

Future researches may reveal how far the phenomenon of "flare-up" *(dissemination in crops) in eczema can be clarified by comparison* with similar events in infections such as tuberculosis It may be that, in addition to specific reactions, temporary non specific changes may be concerned such changes have been thoroughly investigated in haemorrhagic reactions corresponding to the Shwartzman Sanarelli phenomenon

The *fact that epicutaneous reactions do not run parallel with the* serum antihaemolysin titre makes it probable that the reactions *observed in bacterial eczema are of an allergic* and not toxic nature

For a fuller discussion of these see Chapters III and IX *Ed*

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Recent work on autosensitization (see Chapters III and IX) whereby the combination of bacterial products and organ extracts

produces a specific auto-antigen [11] gives promise of increased knowledge of obscure mechanisms in eczema If the presence of bacteria is in fact essential for the development of autosensitivity then the state of exuberant bacterial growth that we have demonstrated in relapsing exudative eczemas certainly provides optimal conditions. Maekawa s[11] hypothesis also deserves consideration. he postulated that organ-specific phosphatides, after addition of antigen could localize the allergic reaction to the corresponding organ. This might furnish an explanation of the increasing polyvalency ("broadening of the allergic base") observed in chronic eczemas. It is conceivable that such phosphatides could be liberated by the activity of cutaneous bacteria and that thereafter other allergens of the most diverse kind could become skin-specific

It is not yet known how far secondary endogenous factors may affect the skin after bacterial eczema has become established; among these may be mentioned foods and products of metabolism. This type of reciprocal relationship between food sensitivity and allergy of infection for instance from infective foci is considered relatively common in urticaria though even here its plac in pathogenesis has not been completely clarified

Focal Infections. Though the relationship between normal skin, eczema and bacteria has by now become partly clear at least as regards cutaneous organisms, the same clarity has not yet been attained concerning eczema reactions to focal infections of the teeth tonsils respiratory and gastro-intestinal tracts etc. Theoretically there is nothing against such a causal relationship and every dermatologist has seen recovery or improvement of a stubborn, recurrent eczema after extirpation of an infective focus. Similarly exacerbations are seen to occur with flare up of foci and with infective disorders of the gastro-intestinal tract. The proof of such clinical impressions is difficult to establish the bacteria of th respiratory and gastro-intestinal tracts are varied the possibilities of microbial products being altered by the secretion of mucus or digestive ferments are highly complicated and there are numerous ways in which such products after absorption could be altered metabolically so as to produce active complex allergens Further focal infections need not necessarily act only allergenically but could also produce eczema in a weakened subject by acting on th neuro-vegetative-humoral system

5. CONCLUSIONS

Experimental and clinical findings enable one to comment on the causative rôle of bacteria in eczema.

Eczematous lesions are often thickly populated with bacteria, with which strongly positive patch test reactions can be elicited. Various strains of *Staphylococcus aureus* and *Streptococcus haemolyticus* are particularly active less commonly strains of *E. coli* and certain saprophytes.

Erythemato-squamous lesions in the exudative stage are particularly rich in bacteria possessing cutaneous activity acute circumscribed mycosiform lesions give similar findings. Acute eczematized neurodermatitis and erythroderma less often show increased bacterial population, while that of dry seborrhoeic eczema, and disseminated erythemato-papular and pityriasiform areas is scarcely different, in type or numbers of bacteria, from normal skin areas. Certain strains of staphylococci and streptococci act selectively in different patients and occasionally activity is shown only by autogenous strains. Specificity of strains of staphylococci can also be demonstrated *in vitro* by agglutination reactions and phage typing. Cutaneous reaction to staphylococci occurs twice as frequently in eczematous as in normal persons; to streptococci four times as frequently The significance of bacteria is shown, *ex juvantibus* by the results of adequate antibiotic therapy and in chronic, recurrent cases sometimes by the results of specific desensitization (*see* Chapter XIII) Although it is often impossible to demonstrate, in a given case, to what extent bacteria have initiated or maintained an eczema, areas that are densely populated with cutaneously active organisms point to a possible microbial cause.

The factor which exerts cutaneous activity is in the protein fraction of the organisms or their products. The eczematous delayed reaction of the bacteria shows a close relationship to the allergy of infection. Experimentally guinea-pigs can be made to develop an eczematous sensitivity to staphylococci or their filtrates which can be elicited on the one hand by repeated inunction, and on the other by intra-cerebral injection of a few drops of filtrate In rare cases progressive eczema can be produced in humans by repeated inunction of cutaneously active bacteria, or eczematous reactions provoked by compresses of live cultures, or old, healed areas can be reactivated in this way

There is as yet no experimental proof as to whether complex allergens of special activity formed in the skin or elsewhere through

produces a specific auto-antigen[1 1 1] gives promise of increased knowledge of obscure mechanisms in eczema. If the presence of bacteria is in fact essential for the development of autosensitivity then the state of exuberant bacterial growth that we have demonstrated in relapsing exudative eczemas certainly provides optimal conditions Maekawa s[11] hypothesis also deserves consideration: he postulated that organ-specific phosphatides, after addition of antigen could localize the allergic reaction to the corresponding organ. This might furnish an explanation of the increasing polyvalency ("broadening of the allergic base") observed in chronic eczemas. It is conceivable that such phosphatides could be liberated by the activity of cutaneous bacteria and that thereafter other allergens of the most diverse kind could become skin-specific

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CHAPTER VIII

SEBORRHOEIC DERMATITIS

G A. GRANT PETERKIN

THE curious term Seborrhoea, an unhappy mixture of Greek and Latin, was unknown to older writers, and the Greeks applied the word Pityriasis to scaly eruptions occurring on the scalp and other parts of the body while authors such as Celsus and the Arabians used Porrigo to describe somewhat similar appearances. Daniel Turner gives this description—"There is yet another disease of the hairy scalp which by the Latins is called Furfuratio and Porrigo from the scurfy or branny scales, extending them all over the said part, and upon scratching being loosened or rising up with the tooth of the comb is named by the common people Dandruff of the head, beard or eyebrows, by the Greeks Pityriasis. Willan and Bateman adopted the name Pityriasis for red and scaly rashes occurring not only on the scalp but also on the trunk. The Viennese school first made current the word Seborrhoea, believing that these scaly lesions were due to inspissated sebaceous material and not to epidermal scales, and thus Hebra divided such manifestations into Seborrhoea oleosa seu adiposa and Seborrhoea sicca seu squamosa. Unna developed this erroneous concept still further and coined the term Seborrhoeic Eczema to cover not only these manifestations but also others probably unrelated. As is said by Ormsby and Montgomery "Though Unna gave eczema seborrhoeicum a wider range than is accepted by the majority of dermatologists, there is little doubt that most of the phenomena he describes under that title are intimately related etiologically and pathologically

It cannot be denied, however that the appellation Seborrhoeic Dermatitis has its uses, so long as the person employing the term realizes that the patient to whom the term is applied may or may not, have overactivity of the sebaceous glands, just as the diagnosis malaria does not imply necessarily any exposure to miasmatic

bacterial colonization, constitute the cause of chronicity intermittent exacerbations and dissemination even through the mechanism of auto-sensitization. Little research has been done into the questions of focal infection secondary sensitization to foods and metabolic products, and the influence of neuro-vegetative-humoral factors in certain cases

At all events the dermatologist would be well advised to consider the significance of bacteria situated on the skin and in internal foci in the diagnosis and treatment of eczema

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which spread and coalesce to form erythemato-squamous patches with greasy yellow scaly centres. This greasy appearance is not so obvious in some types, particularly if the rash has extended to involve the limbs. The eruption which shows a tendency to ringed oval or gyrate patches is not usually very itchy but pruritus may be a feature if the spread is rapid and extensive.



FIG. 45
Seborrhoea Corporis—eczématide figurée stéatoïde.

4 SEBORRHOEIC DERMATITIS OF THE SCALP AND FLEXURES (Flexural Infective Eczema)

As H G Brooke said, "the view which we take of the connection of seborrhoea with eczema depends entirely on our conception and definition of the meaning of eczema. Whatever views we hold as to the differentiation of artificial dermatites, we

odours As Sir Norman Walker[4] put it "It is a mere dialectic device to point triumphantly to the derivation of the word and claim this in support of any theory for those who were responsible for the coining of the term were under the impression that the scales of seborrhoea were the dried secretion of the sebaceous glands which they are not Seborrhoea should I believe, be looked on as a specific form of inflammation of the skin mainly occurring on the scalp and spreading from there to other places." Many first-rate dermatologists are convinced that there is such a thing as the seborrhoeic diathesis and there is much to be said for this point of view The character of the fruit depends to a large extent on the soil

Thus strictly speaking, the term Seborrhoeic Dermatitis should only be used for a condition in which there is an increased oily secretion from the sebaceous glands, but through use and wont it is also applied to the scaly conditions described under that heading.

CLASSIFICATION OF SEBORRHOEIC DERMATITIS

1 Seborrhoea Oleosa

(*Syn* —Seborrhagia Steatorrhoea Flux Sebacea)

This is the true oily seborrhoea which can be seen typically in young infants at puberty sometimes after the menopause and occasionally in association with Parkinsonism

2 Pityriasis Simplex Capitis

(*Syn.*—Dandruff)

This is found in a high proportion of normal individuals, and occurs as dry scaly flakes without any redness of the scalp and usually little or no itching.

3 Pityriasis Corporis

(*Syn* —Seborrhoea Corporis, Flannel Rash)

By Darier this group has been christened **Eczématides** and subdivided as follows —

(*a*) Eczématides figurées stéatoides (Fig 45) (Seborrhoea Corporis of Duhring flannel rash)
(*b*) Eczématides Psoriasiformes.
(*c*) *Eczématides Pityriasiformes* (Fig. 46)
(*d*) Eczématides à type de Pityriasis Rosea

Pityriasis corporis is most typically seen on the skin of the presternal or inter-scapular regions It begins as small red papules

which spread and coalesce to form erythemato-squamous patches with greasy yellow scaly centres. This greasy appearance is not so obvious in some types, particularly if the rash has extended to involve the limbs. The eruption which shows a tendency to ringed oval or gyrate patches is not usually very itchy but pruritus may be a feature if the spread is rapid and extensive.



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practically call all eruptions eczema which show the punctate oozing of coagulable serum or its results in the form of crusts. Seborrhoeic Dermatitis *of the scalp and flexures is the only one of* these groups which can genuinely be said to be eczematous in character though lesions of Pityriasis Corporis can become eczematized *On the scalp and in the folds can be seen an inflam-*

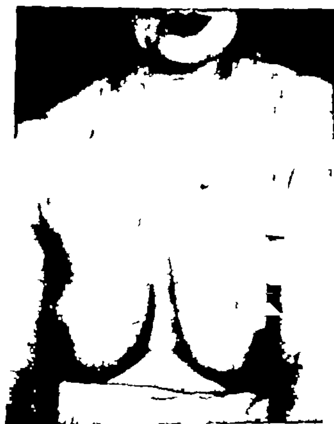


FIG. 46
Extensive Seborrhoea Corporis—eczématide pityriasiforme

matory process characterized by redness, exudation and crusting, with the typical " eczema pits " (Figs. 47 and 48)

Though this eruption may originate from a Pityriasis Capitis (perhaps following trauma with a comb used to remove the dandruff) or a Pityriasis Corporis affecting the flexures (Fig. 49) most frequently the first evidence of it is a fissure deep in the fold from which the rash spreads so that eventually large areas such as the whole of the scalp may be involved (Fig 50) It can thus occur in subjects with a previous history of " seborrhoeic " manifestations but may also occur in those with no prior evidence of any cutaneous



FIG. 47
Flexural Seborrhoeic Dermatitis of child



FIG. 48
Flexural Seborrhoeic Dermatitis of adult.

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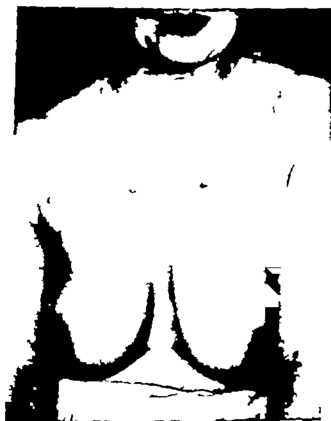


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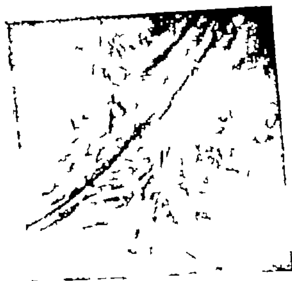


FIG. 48
Flexural Seborrhoeic Dermatitis of adult.

abnormality This is one of the sound reasons why some dermatologists consider that the name seborrhoeic dermatitis should be abandoned.

Blepharitis is a common form of flexural lesion and often is first noticed after an attack of measles



FIG. 49

Left axilla, showing eczématides tending to change into a streptococcal dermatitis. This patient had pityriasis capitis, seborrhoea corporis of the trunk and flexures, and an exudative dermatitis of th groins.

5 Follicular Seborrhoeic Dermatitis

When a folliculitis predominates, one may find either *Seborrhoeic Sycosis* or *Bockhart's Impetigo* affecting respectively the beard area and the limbs Most of the lesions are follicular papules and pustules but honey-coloured crusts due to streptococcal infection and patches of papulo-vesicular eczema may also be present, particularly in chronic cases Such cases are seen in debilitated individuals and in miners working in wet dirty conditions

AETIOLOGY It must be confessed that the exact causation of the various forms of Seborrhoeic Dermatitis is still obscure, and it seems possible that eventually it will be proved that the basic cause lies in some dietetic deficiency of which we are not yet aware. The recent paper by Hodgson-Jones, MacKenna and Wheatly* on the surface skin fat in seborrhoeic dermatitis may point the way



FIG. 50
A typical case of streptococcal seborrhoeic dermatitis of scalp and ears.

towards the solution of this aetiological puzzle. They showed that the composition of the sebum in these cases was altered as a whole, without a simple deficiency or excess of any one constituent; in particular there appeared to be a derangement of the metabolism of squalene and cholesterol. The authors prudently remark that at present we cannot decide whether these changes play the part of cause or result. It should be kept in mind that many people who show stigmata of the seborrhoeic state never develop seborrhoeic dermatitis, and that it is possible that all of mankind are potential subjects for seborroeic dermatitis if subjected to the stresses necessary to provoke the disease.

The following are some of the factors which may play a part in the production of the complaint.

Heredity Not infrequently one can obtain a history that a close relation of the patient has had a similar dermatosis with precisely the same texture and type of skin, though it is rare to find such

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FIG. 49
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recovered from normal scalps and in other scaly conditions such as Psoriasis. MacLeod and Dowling, using what they believed to be whole cultures of the Pityrosporum, succeeded in producing on excoriated skin lesions very similar to the eczematides; later they realized that the organism used was a yeast-like one but not the Pityrosporum. Bigham found that he could recover the organism from almost every scalp including twenty controls. Martin-Scott, in thorough animal and human experiments, discovered that positive cultures were much fewer in cases of seborrhoeic dermatitis where active inflammation was present, but easily obtained in cases labelled Pityriasis capitis and in the other more chronic seborrhoeic manifestations (3 per cent. in acute cases as compared with 46·4 per cent. in the chronic lesions). An interesting point was that the organism was not cultured from the scalps of normal infants, but was grown from six of the nine cases with infantile eczema. He noted that it appeared to be non-pathogenic to laboratory animals and that human experiments indicated it to be a non-pathogenic saprophyte failing to fulfil Koch's postulates.

Staphylococci. It was pointed out by Martin-Scott that in cases of seborrhoeic dermatitis with active inflammation the commonest organism cultured was a penicillin-sensitive, coagulase negative white staphylococcus, which seemed to suggest that either these cocci had an inhibitory action on the pityrosporum or that the presence of the latter encouraged the growth of the cocci, but stroke cultures of both on the same plate disproved any symbiotic or antibiotic action. It seems possible, however, that some alteration in the *p*H of the skin might have rendered it a better culture medium for the staphylococcus and a poorer one for the yeast-like organism.

Staphylococcus aureus can often be found in lesions associated with seborrhoeic dermatitis, such as seborrhoeic sycosis, blepharitis and furunculosis (*e.g.* of the nape of the neck) and seems to be a secondary aggressor.

Streptococci. In moist flexural eruptions, particularly with fissuring, *Str. pyogenes* can usually be recovered, though in some patients, especially middle-aged women, the yeast *Candida albicans* may be found. The streptococcus can also be obtained from red exudative scalps. Kinnear[13] who considers flexural eczema, or as he terms it "streptococcal dermatitis" entirely distinct from seborrhoeic dermatitis, found in these cases a non-haemolytic streptococcus, while in impetigo he invariably cultured a haemolytic

clear-cut evidence as in cases of the asthma-eczema syndrome (atopic dermatitis)

Climate and Race. It would appear that the tendency to Seborrhoeic Dermatitis is more evident in peoples living in the temperate zones, particularly in Northern Europe, so that it is more often seen in Britain, France Germany and Scandinavia than in the Latin races During the war in Italy there were engaged soldiers from many different races e g the British Empire (including the United Kingdom Canada South Africa New Zealand, Australia India East Africa etc) U.S.A France, Poland Brazil Jugoslavia Italy Germany and Russia There was no doubt that seborrhoeic dermatitis occurred much more frequently in troops from Britain and Canada than from any of the other countries—so that race and diet were the only etiological factors not common to all.

Diet. The similarity between Vitamin B complex deficiency induced experimentally in animals and the clinical findings in seborrhoeic dermatitis of the flexures gave rise to fond hopes that the administration of the complex would cure the disease, but these have been disappointed though in some cases great improvement follows the administration of Vitamin B in such a form as crude liver injections. Seborrhoeic manifestations are often seen in malabsorption states and in drug rashes such as those due to sulphonamides and gold which again seems to indicate a deficiency of absorption or in the diet

Endocrine. Certain stages of life may be accompanied by a greasy skin with hyperactivity of the sebaceous and sweat glands Thus the young baby may develop a seborrhoeic dermatitis of the scalp and the young person at puberty may be similarly affected In post-menopausal women it is not uncommon to find seborrhoeic manifestations, some even developing what is clinically a true acne vulgaris such as is seen after puberty

Local Infection. Three groups of organisms have been incriminated as playing parts in the production of the various forms of Seborrhoeic Dermatitis — *Pityrosporum ovale (Pityrosporon of Malassez) Staphylococci (Staphylococcus aureus + albus)* and *Streptococci* both haemolytic and non-haemolytic

Pityrosporum Ovale a yeast-like bottle-shaped organism was for long considered to be the infective agent in Pityriasis capitis and Pityriasis corporis, though it was recognized that it could be

those which contain paraphenylenediamine, *e g* Inecto Rapid, shampoos; cold wave perms," etc.

(*b*) In the *flexures* fissured and eczematous reactions may be due to such things as spectacle limbs; rubber earphones; garments, *e g* dyed dresses, khaki shirts, and detergents left in the material after washing; depilatories; rubber dress-protectors; anti-perspirants, vaginal douches; quinine and rubber contraceptives, etc



Fig 51
Arm, showing drug eruption due to phenobarbitone, resembling seborrhoea corporis.

(*c*) On the *trunk*, eczématides can be simulated by discrete patches due to contact with nail-varnish on the neck and upper trunk, and by underwear especially when processed with a stiffening or anti-shrink chemical.

2. Asthma-eczema (Besnier's Prurigo; Atopic Dermatitis). In infancy it may be impossible to tell whether the patient will in later life develop a tendency to seborrhoeic dermatitis or to asthma-eczema, as what appears to be a typical seborrhoeic dermatitis in a small child may gradually drift into a Besnier's Prurigo

(*a*) The *scalp* is not usually involved in asthma-eczema, but sometimes a thick dry dandruff is found.

(*b*) The lesions in the *flexures* tend to be dry papular and lichenified, and the folds chiefly involved are the bends of the arms and legs, the front of the wrists, and the neck

one In other people's experience, either or both types of streptococci can be isolated from flexural fissures

Focal Sepsis. It has been remarked by many authors that focal sepsis can be discovered in an extraordinarily high proportion of cases of seborrhoeic dermatitis, particularly the flexural type. In a consecutive series of sixty two cases of seborrhoeic sycosis investigated by Ingram[1] infected antra were found in 72 per cent., but it is difficult to assess whether these patients were prone to both the seborrhoeic sycosis and the antral infection or whether the infected antra helped to precipitate the skin condition Indubitably one can recover pathogenic staphylococci or streptococci from the nasal passages of the vast proportion of people with flexural seborrhoeic dermatitis and seborrhoeic sycosis.

Relation to the Asthma-eczema Syndrome (Atopic Dermatitis). It is the exception to find a history of asthma or related diseases in seborrhoeic dermatitis but these exceptions do occur and some cases which clinically are typical cases of seborrhoeic dermatitis often of a resistant nature may be associated with such a manifestation as asthma and be caused for instance, mainly by a sensitization to a food such as milk. Likewise, one may observe an infant with what appears to be a typical seborrhoeic dermatitis of the scalp and ears gradually alter till it becomes a characteristic case of *Besnier's Prurigo*

Psychosomatic Factors. In these days it is fashionable to hold the view that most, if not all skin diseases are provoked by or associated with psychological causes, but there is little doubt that such factors are highly important in this dermatitis In his paper on *seborrhoea Brooke remarked "I am not upholding* the exclusive microbic origin of eczema and until better explanation is found I can only explain certain outbreaks as neurotic or due to abnormal neurotic reflexes Among the many dermatologists who wish to adhere to an exact definition of seborrhoeic dermatitis Becker and Obermayer classify the flexural type under the neurodermatoses Wittkower[1] found that patients tended to develop an *attack of seborrhoeic dermatitis following incidents affecting* either their social status or their self-esteem

DIFFERENTIAL DIAGNOSIS

1 Contact Dermatitis. *(a) On the scalp reactions very like* seborrhoeic dermatitis can be produced by hair dressings, such as violet oil quinine and Vaseline hair tonics dyes especially

5. **Psoriasis.** The link between psoriasis and seborrhoeic dermatitis is a close one and time and again one sees patients whose skin condition at one period may be diagnosed as a typical seborrhoeic dermatitis and on examination a year or so later may be a genuine psoriasis. Flexural psoriasis is particularly closely related and was called by Unna Psoriasis-seborrhoea, as the dermatosis seems to be compounded of both diseases. Occasionally the psoriasiform type of eczématide gradually changes to a true psoriasis. Histologically the section of what appears to be a seborrhoeic dermatitis may show the picture of psoriasis.

6. **Pityriasis Rosea.** (*a*) The *scalp* in this disease, especially in children, may show dry oval patches quite unlike pityriasis capitis.

(*b*) The *flexures* are rarely involved, unlike seborrhoea corporis.

(*c*) On the *trunk* it is often impossible to distinguish the pityriasis rosea-type of seborrhoea corporis from the disease itself but in a characteristic case the herald patch, and the dry oval pink patches *with their collarette* along the lines of cleavage of the skin aid the diagnosis.

7 **Lichen Planus.** The lilac flat-topped papules of this disease and the presence of lesions on the mucous membranes should make diagnosis plain.

8. **Syphilis.** (*a*) On the *scalp* the corona veneris often seems to be associated with some seborrhoeic dermatitis, but the distinctive reddish-brown colour and the positive serology are diagnostic.

(*b*) In the *flexures* moist papular lesions may simulate a seborrhoeic dermatitis.

(*c*) On the *trunk* maculo-papular roseolar annular serpiginous and psoriasiform syphilides may imitate to some extent a seborrhoea corporis.

9 **Parapsoriasis en Plaque.** This rare condition is often originally diagnosed as a seborrhoea corporis, but its long duration, its lack of itching and resistance to ordinary treatment should rouse suspicion of the diagnosis.

Histology

As one can imagine, when a term such as seborrhoeic dermatitis covers such protean manifestations, the histological picture must vary considerably and there is not one which can be said to be diagnostic. Darier gave the name eczématides to what is called seborrhoea corporis, as the macroscopic appearances were so nearly those of an eczema. In acute inflammatory forms, and in some

(c) Usually the upper part of the *trunk* like a child's bib is affected but not infrequently eczématides are also present.

3 Drug Eruptions. Many drugs, but particularly gold, arsenic and mepacrine (atabrine) can provoke reactions indistinguishable from seborrhoeic dermatitis, either as eczematides or as flexural

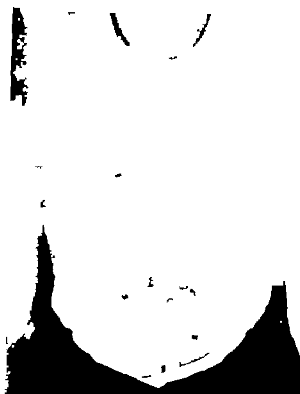


FIG. 5
Upper trunk tinea corporis simulating seborrhoea corporis

lesions, *e g.*, retroauricular eczema Of other drugs the barbiturates are the most likely to produce eczématides (Fig. 51)

4 Fungus Infections. (*a*) On the *scalp* tinea capitis and favus is easily diagnosed, confirmation being obtained by inspection under a Wood's light and by microscopic and cultural examination.

(*b*) In the *flexures* tinea cruris et axillae does not usually commence deep in the fold of the skin and is dry and scaly with a clear-cut spreading edge Infections due to the yeast *Candida albicans* on the other hand cannot be distinguished clinically from the streptococcal infection

(*c*) On the *trunk* either a tinea corporis or a dermatophytide can mimic a seborrhoea corporis extremely closely (*see* Fig. 52)

states of anxiety stress and strain; employment in hot dusty atmospheres, as mining; and absence of light and fresh air are conditions which the seborrhoeic will not readily tolerate." With these remarks the writer is in hearty agreement and believes that some time in the future the basic cause will be discovered and that this cause will be found to be a dietetic deficiency perhaps even of a trace metal. Why else are the British people so much more liable to the various manifestations of seborrhoeic dermatitis than those of the U.S.A.?

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chronic cases the stratum corneum contains vesicles, and cocci can be seen in numbers In the average case affecting the scalp and the flexures, hyperkeratosis parakeratosis and some acanthosis are present, with a certain amount of oedema and perivascular infiltrate. The sweat and the sebaceous glands show no pathological changes (*see also* Chapter V—*Ed*)

SUMMARY

The name seborrhoeic dermatitis is unfortunate but to some extent has been sanctified by the passage of time Many dermatologists feel that the appellation should be abolished, but so far no entirely satisfactory alternative names have been forthcoming for the several diseases grouped under the term The purists rightly consider that the name should be applied only to skin conditions where there is actual increase of sebaceous secretion, that seborrhoea corporis should be described as an eczématide, and that the exudative flexural type should be re-classified as an infective eczema *e g* streptococcal dermatitis, or as a neuro-dermatitis. It cannot be denied that in a high proportion of patients with flexural eczema there is no evidence, either from the history or from the clinical appearance of an excessive secretion of sebum but in many other cases thorough questioning will reveal links in the chain. In his lifetime, a patient may be affected by different forms of seborrhoeic dermatitis. For instance a man aged twenty-six was referred for treatment of a seborrhoeic sycosis and a dry scurfy scalp In infancy he had had an eczema affecting his scalp and ears at the age of nineteen he had a profuse oily dandruff and a greasy skin when twenty-one, he was affected by a dermatitis of his axillae and groins Here, then is a man who has had (1) an infantile seborrhoeic dermatitis, (2) a seborrhoea oleosa (3) a flexural seborrhoeic dermatitis, and (4) a pityriasis capitis and a seborrhoeic sycosis with no apparent greasiness of the skin

As Ingram wisely states "It will be seen that the greasy skin of the seborrhoeic is but one small indication or reflection of a constitutional state or diathesis which is of considerable importance and the eruptions which we dub seborrhoeic are in fact reflections of disturbances of the constitutional state rather than infective conditions peculiar to the skin While circumstances of health employment, and environment generally may do much to promot the seborrhoeic state, this diathesis is probably an inherited one in the vast majority of cases States of poverty and malnutrition,

metabolic, endocrine or nervous factors could be abandoned forthwith. This is not to say that such factors would play no part in the production of disseminated eczema. It would however relegate them to a rôle of secondary importance.

We have seen how the genesis of contact eczema can be followed step by step and how most of its phenomena can now be explained on the basis of observed fact; the only gap in our knowledge applies equally to most problems in the field of Medicine: what is the individual factor which predisposes only a certain proportion of subjects to this condition? If Adamson's view is correct and every case of extensive eczema represents the dissemination of the disease from a primary focus, then a true endogenous eczema simply does not exist; it would follow then, that there is no need to search for vague constitutional factors any more than there is in, say, contact eczema.

In an attempt to confirm or disprove Adamson's view I have recently analysed 100 cases taken alphabetically from my records. All these patients presented themselves with an extensive, symmetrical, papular or papulo-vesicular eczema. In some of those cases originating from a primary cutaneous focus it was not possible to be certain of the nature of the original lesion, but in most there was visible evidence of its pathogenesis, confirmed by patch test in those of contact eczema. Nevertheless, the enquiry is primarily concerned with the presence or absence of a preliminary skin lesion, and only secondarily with its precise nature.

TABLE VIII

METHOD OF ONSET OF 100 CASES OF EXTENSIVE, SYMMETRICAL ECZEMA

A From primary cutaneous focus		80
1 Contact Eczema	31	
2 Bacterial infection (including seborrhoeic eruptions)	27	
3 Combination of (1) and (2)	7	
4 Lichen simplex chronicus	5	
5 Hypostatic (varicose) eczema	5	
6 Tick infestation		
7 Severe sunburn	2	
8 Acute fungous infection (eczematous)	1	
B Drug Eruption (Penicillin)		1
C Unexplained, apparently spontaneous		19
TOTAL		100

CHAPTER IX

DISSEMINATED AND ENDOGENOUS ECZEMAS

L. J. A. LOEWENTHAL

CERTAIN widespread symmetric eruptions have now been considered these comprise contact eczema involving extensive areas, atopic dermatitis and some types of seborrhoeic dermatitis If these be excluded there still remain numerous cases of symmetrical eczema usually affecting large areas, whose development and course suggest an internal origin reminiscent of an exanthem It is not surprising that a constitutional condition, the *eczéma vrai* or *eczéma-maladie* of the French is so frequently postulated. It is, in fact, possible that such an entity exists but recent work makes it ever less probable that it is the direct outcome of the diathetic, endocrine and nervous influences which are usually blamed

Preliminary Considerations. It has for long been known that a localized patch of eczema of any kind may be the first manifestation of a generalized eruption. This phenomenon of *dissemination* has aroused considerable interest it has been referred to in previous chapters and is of fundamental importance in much of the modern work to be reviewed

Even in some of the older text-books it is noted that a primary irritant dermatitis such as that produced by Hebra's croton oil experiment, may cause fresh patches of eczema to appear at a distance. Noting therefore, that a single lesion may herald a generalized eczematous outbreak it is reasonable to enquire what proportion of cases of generalized eczema develop in this way In Adamson's experience, every case in which the history was traced back to the beginning was found to have commenced after the application of some local irritant or allergen or as an eczematized impetigo or seborrhoeic eczema If this statement could be verified then the concept of an eczema arising *de novo* as the result of toxic

response to the presence of the organism in sensitized tissue. This may represent a form of immunity very probably so in view of the rapidity with which the organism is destroyed but the consideration of this question is irrelevant here. Though these lesions are typically the response to living organisms, it is still possible that in some cases they may represent a reaction to microbial products only. It is certainly true that eczematous eruptions have been produced repeatedly by applying sterile culture filtrates as patch tests (see Chapter VII).

Although "id" eruptions from hyphomycetes had been described previously the eczematous type, secondary to tinea of the feet or other areas of the glabrous skin, was first given prominence by Williams. Since this publication the number of cases of "epidermophytid" has become enormous; it is apparent, in fact, that this diagnosis is made far too frequently in some countries and on quite insufficient grounds. Nevertheless, it can be accepted that eczematous eruptions, not only of the hands, may appear as an "id" reaction to active eczematous fungal lesions of the feet or elsewhere. An observation possibly of practical importance, remains to be stated: in animal experiments it has repeatedly been shown that the site of the "id" eruption may be determined by minimal superficial trauma, such as that produced by shaving. This has some bearing on the clinical manifestations of disseminated eczema which will be discussed later.

Bacterids

An obvious step from the proved eczematous "id" eruptions of fungous infection is to the bacterid. There has been much difference of opinion here, possibly because of the difficulty of proving the pathogenic or allergenic properties of bacteria normally resident on the skin. The French school has long insisted that the sharply demarcated scaly patches which Darier called *eczématides* are always microbial in origin. Bloch[a] and Sabouraud also regarded micro-organisms or their toxins as potential allergens and specifically included bacterids among eczematous manifestations. Chapter VII demonstrates how much further this concept has been taken by modern workers.

These bacterid eruptions cannot be distinguished clinically or histologically from other disseminated eczemas; though they may imitate the parent lesion and present only red, sharply demarcated patches, they may readily show as papules or vesicles, grouped or scattered (Fig. 53).

COMMENT (TABLE VIII)

1 The primary cutaneous focus was present for periods varying from a week to several years before the onset of the generalized eruption.

2. If there is such a condition as primary endogenous eczema (*ec ème vrai eczéma-maladie*) it could conceivably begin as an initial lesion in that case it might include some patients listed under A2, where such a hypothetical lesion had become secondarily infected, as well as under C. That this is unlikely is shown by the large number of cases in A2 whose origin was demonstrably an infective eczema supervening on banal irritations *such as follicular impetigo boot chafes*, and so on.

3 With regard to Group C it will be remembered that Adamson specified only those cases whose history was traced back to the beginning *In the nineteen patients under review here there is no certainty* that such was the case Routine history taking can be fallible through errors of omission by doctor and patient alike An episode of eczema *in infancy or childhood may well be unknown to the patient in other* cases the mention of previous attacks may even be voluntarily suppressed This actually occurred in four of the cases in A1 presenting an *apparently spontaneous outbreak of eczema they stoutly denied a history* of previous skin trouble yet reference to their employment records showed that they had suffered from contact eczema from topical medica*tion several years previously This contact eczema had in each case been* followed by secondary dissemination

This leads us to a generalization of great practical importance: *Once disseminated eczema has supervened on a primary lesion it may continue to re-appear apparently spontaneously without the development of a further primary lesion*

DISSEMINATED ECZEMA

In this section will be considered all those eczemas in which substances presumably allergenic are absorbed from a primary eczematous focus and conveyed to distant parts. The work of Haxthausen and others reviewed in Chapter III has made the reader familiar with this concept; it will here be considered in a more systematic way

DERMATOPHYTIDS

The " id " or " ide " suffix was originally proposed by Darier to designate certain characteristic *skin lesions in tuberculosis and* was later applied to other infectious diseases. At first because of inability to recover organisms from these lesions, they were thought to be caused solely by non-living microbial products Later work however has shown that the micro-organism itself is in most cases brought to the skin the " id " reaction is probably an allergic

traces so small as to be practically beyond chemical detection regularly produced eczematous reactions.

In this connection we should also recall the experiments of Percival and others. It can be shown, with a fair degree of probability that the generalized eczema reaction can be produced (in sensitized individuals) by a proportionately smaller quantity of *circulating* antigen than the minimum amount required to evoke a positive reaction by *external* application.

In this type of generalized eczema, then there appear to exist all the requisite conditions for the development of an "id" eruption: a primary focus leading to sensitivity of the whole epidermis; the possibility of absorption of the allergen into the blood stream; and interaction of this allergen, admittedly in almost incredibly minute quantity with the previously sensitized epidermis in any area. That this hypothesis is not the only one which will account for the observed facts has been shown in the discussion on bacterids, for dissemination from a focus of contact eczema could equally be attributed to bacterial infection of such a focus. This uncertainty is reflected in Table VIII where seven cases are listed as "a combination of contact eczema and bacterial infection."

The dissemination of a contact eczema sometimes follows a peculiar pattern which was frequently seen in the days when sulphonamide dressings were freely used for minor infections of the skin. The first example of this *contra-lateral symmetrical "id"* which came to my notice will serve as a description applicable to many others.

A soldier was admitted to hospital with a sulphonamide contact eczema around an ecthymatous sore on the flexor surface of the *right* forearm. When I first saw him a few papules were visible on precisely the same part of the left forearm, where there was no possibility of contact with sulphonamide. The following day these papules had developed into an eczematous plaque of the same size and very nearly the same rectangular shape as the original lesion. A few days later the generalized eruption began to appear.

A similar mechanism may account for a finding in many cases of vesicular eruption of both feet. In these, direct microscopic examination of blister tops from one foot will show *abundant fungal elements* while those from the other foot are negative. It seems reasonable to postulate that such subjects are presenting a contra lateral symmetrical "id" eruption. Two further examples suggest that this phenomenon is not limited to eczematous eruptions: *Goldsmith* quotes cases of prurigo aestivalis in whom irradiation of one arm produced exacerbation of symptoms equally in both arms. In a case of cold urticaria reported by me areas sprayed with ethyl chloride showed no whealing, but this occurred promptly and consistently on the symmetrically opposite site.

CHEMICAL "IDS"

It is reasonable to wonder whether substances other than the *products of living organisms* can act in this way The main objection to this hypothesis can be reduced to a simple question of quantity living microbes continue to produce their allergens, but an inert chemical applied to *the skin cannot reproduce itself* Nevertheless Sulzberger[7] states that there is some evidence that contact



FIG. 53
Papulo-vesicular bacterid eruption. The primary focus was an eczematous area complicating furunculosis of the axilla.

eczema of the feet, for instance from shoe leather or medicaments, can produce a secondary eczema of the hands and *vice versa* If this phenomenon which I can confirm from personal experience is actually comparable to the "id" eruptions caused by micro-*organisms, then there is no reason why these secondary* eruptions should be limited to the extremities In other words, the generalized outbreaks so often seen to occur in cases of contact eczema could be explained as "id" eruptions due to the absorption and dissemination through the blood stream of the allergenic substance *even if this be a relatively simple, inorganic chemical* Ravaut was among the first to postulate such a chemical "id" eruption and even gave the name "*javellide*" to the secondary eczematous eruption following contact eczema with Eau de Javelle (sodium hypochlorite solution)

The objection *that this is unlikely in view of the minute quantities* which could be disseminated in this way falls away when we consider some examples *quoted in Chapters II and III* in these

The word "autosensitization" was coined by Whitfield[44] to explain three different phenomena, of which only one concerns us here. His own words are best used to present his ideas.

Rubbing of a patch of dry thickened eczema sometimes produces a generalized eruption, at first a punctate erythema but soon becoming a papulo-vesicular eczema."

"Again (in) a patch of varicose eczema owing to application of unsuitable treatment there may occur suddenly a generalized eruption all over the base of the neck, the chest and the arms."

I regard then both of these as instances of extended or generalized eruption, respectively due to the absorption of the patient's own broken down tissue products, and I believe also that this is the mechanism by which an eczema produced by external irritants such as hair dye, etc., extends far beyond the original site of application and often appears in remote parts such as the flexures of the elbows, the inguinal and the submammary regions, etc."

This concept has been enthusiastically supported by many Milbradt reported finding sensitivity to human skin in certain human beings, and Ingram went so far as to state that autosensitization is an aetiological factor in every case of eczema. Templeton and his co-workers claim to have produced precipitins to skin extract in five volunteers after four injections of this extract; no added bacterial toxin was used. Cormia and Esplin tested patients suffering from "autoeczematization" with skin and other extracts; positive wheal reactions were obtained in many cases, not only to scale extracts, but to blister fluid and leucocyte suspensions. The last suggested to them that autosensitization occurring during X-ray therapy of eczematous areas may be caused by the release of proteolytic enzymes from destroyed leucocytes. Deductions based on this work must necessarily be tentative, as only urticarial, and not eczematous reactions were demonstrated. The same objection attaches to the work of Hampton and Cooke,[44] who obtained similar positive tests with human dander extract and demonstrated the presence of passive transfer antibodies. As the reader will recall, this finding is at variance with our concept of non-atopic eczema.

Hopkins and Burky though concerned primarily with eczema of the hands, suggested a sensitization to a combination of the patient's own keratin and staphylococcus toxin. From every point of view this is a reasonable hypothesis, for it at once co-ordinates clinical with laboratory findings. Further it offers an acceptable compromise between the pure bacterid hypothesis and the pure autosensitization concept of Whitfield. At this stage of our

AUTOSENSITIZATION

We have now traced the development of disseminated eczema from systemic spread of fungal bacterial and chemical allergens. The last hypothesis to be considered is the possibility of the skin itself acting as an allergen under certain conditions; Epstein's hypothesis of the development of "protigen" was mentioned in Chapter III and becomes relevant again here

The history of early investigation into organ-specific antibodies has been well summarized by Sulzberger[11] modern work dates from the now classical experiment of Burky and Woods.[12] Combining rabbit lens or muscle extracts with staphylococcus toxin and using this mixture as an antigen these workers were able to demonstrate the production of antibodies to lens or muscle in normal rabbits. In rabbits so prepared minor traumata to the lens or to muscle then produced local reactions far exceeding those elicited in unprepared, control rabbits Omitting many further experiments showing the existence of organ-specific antibodies to brain kidney and hormones we come to the first demonstration of anti-skin antibody by Hecht, Sulzberger and Weil[13] Using rabbits, and substituting rabbit skin extract for lens or muscle, alone with staphylococcus toxin these workers were able to demonstrate the formation of precipitins to homologous skin. Although the final step of producing cutaneous lesions by minor trauma was not attempted in this experiment, analogy with much other work makes it at least probable that positive results will be obtained in this way The new horizon which such studies reveal in the pathogenesis of disseminated eczemas are best summed up in Sulzberger's words '

"Is it not possible that damage to the skin (either through infection or through physical agents or through reactions to allergens) may create and liberate skin antigens which, in turn produce skin specific antibodies which in turn, produce reactions in the skin itself wherever and whenever skin antigen is made available and accessible to their action? Would not this hypothesis explain—perhaps better than all others—the recognized fact that after an eczematous response has been produced in one area there often follow months and years during which not only the areas of exposure, but also almost all other skin sites react with pathologic responses to all manner of forces and substances previously innocuous and previously tolerated?"

This postulate, that the subject can be primed with antibodies to his own skin and thereafter react with eczematous lesions to the most banal stimuli transports us in a single stride from laboratory to clinic.

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CERTAIN widespread symmetric eruptions have now been considered these comprise contact eczema involving extensive areas atopic dermatitis and some types of seborrhoeic dermatitis If these be excluded there still remain numerous cases of symmetrical eczema usually affecting large areas, whose development and course suggest an internal origin reminiscent of an exanthem It is not surprising that a constitutional condition the *eczéma vrai* or *eczéma-maladie* of the French is so frequently postulated. It is in fact, possible that such an entity exists, but recent work makes it ever less probable that it is the direct outcome of the diathetic, endocrine and nervous influences which are usually blamed.

Preliminary Considerations. It has for long been known that a localized patch of eczema of any kind may be the first manifestation of a generalized eruption. This phenomenon of *dissemination* has aroused considerable interest it has been referred to in previous chapters and is of fundamental importance in much of the modern work to be reviewed

Even in some of the older text-books it is noted that a primary irritant dermatitis, such as that produced by Hebra's croton oil experiment, may cause fresh patches of eczema to appear at a distance. Noting therefore, that a single lesion may herald a generalized eczematous outbreak it is reasonable to enquire what proportion of cases of generalized eczema develop in this way In Adamson's[2] experience every case in which the history was traced back to the beginning was found to have commenced after the application of some local irritant or allergen or as an eczematized impetigo or seborrhoeic eczema If this statement could be verified then the concept of an eczema arising *de novo* as the result of toxic

metabolic, endocrine or nervous factors could be abandoned forthwith. This is not to say that such factors would play no part in the production of disseminated eczema. It would, however relegate them to a rôle of secondary importance.

We have seen how the genesis of contact eczema can be followed step by step and how most of its phenomena can now be explained on the basis of observed fact; the only gap in our knowledge applies equally to most problems in the field of Medicine: what is the individual factor which predisposes only a certain proportion of subjects to this condition? If Adamson's view is correct and every case of extensive eczema represents the dissemination of the disease from a primary focus, then a true endogenous eczema simply does not exist; it would follow then, that there is no need to search for vague constitutional factors any more than there is in say contact eczema.

In an attempt to confirm or disprove Adamson's view I have recently analysed 100 cases taken alphabetically from my records. All these patients presented themselves with an extensive, symmetrical, papular or papulo-vesicular eczema. In some of those cases originating from a primary cutaneous focus it was not possible to be certain of the nature of the original lesion but in most there was visible evidence of its pathogenesis, confirmed by patch test in those of contact eczema. Nevertheless, the enquiry is primarily concerned with the presence or absence of a preliminary skin lesion, and only secondarily with its precise nature.

TABLE VIII

METHOD OF ONSET OF 100 CASES OF EXTENSIVE, SYMMETRICAL ECZEMA

A. From primary cutaneous focus		80
1. Contact Eczema	31	
2. Bacterial infection (including seborrhoeic eruptions)	27	
3. Combination of (1) and (2)	7	
4. Lichen simplex chronicus	5	
5. Hypostatic (varicose) eczema	5	
6. Tick infestation	2	
7. Severe sunburn	2	
8. Active fungous infection (eczematoid)	1	
B. Drug Eruption (Penicillin)		1
C. Unexplained, apparently spontaneous		19
TOTAL		100

Comment (Table VIII)

1 The primary cutaneous focus was present for periods varying from a week to several years before the onset of the generalized eruption.

2. If there is such a condition as primary endogenous eczema (*eczéma vrai eczéma maladie*) it could conceivably begin as an initial lesion in that case it might include some patients listed under A2, where such a hypothetical lesion had become secondarily infected as well as under C. That this is unlikely is shown by the large number of cases in A2 whose origin was demonstrably an infective eczema supervening on banal irritations such as follicular impetigo boot chafes, and so on.

3 With regard to Group C it will be remembered that Adamson specified only those cases whose history was traced back to the beginning. In the nineteen patients under review here there is no certainty that such was the case Routine history taking can be fallible through errors of omission by doctor and patient alike An episode of eczema in infancy or childhood may well be unknown to the patient, in other cases the mention of previous attacks may even be voluntarily suppressed This actually occurred in four of the cases in A1 presenting an apparently spontaneous outbreak of eczema they stoutly denied a history of previous skin trouble yet reference to their employment records showed that they had suffered from contact eczema from topical medication several years previously This contact eczema had in each case been followed by secondary dissemination

This leads us to a generalization of great practical importance. *Once disseminated eczema has supervened on a primary lesion it may continue to re-appear apparently spontaneously without the development of a further primary lesion.*

DISSEMINATED ECZEMA

In this section will be considered all those eczemas in which substances presumably allergenic are absorbed from a primary eczematous focus and conveyed to distant parts. The work of Haxthausen and others reviewed in Chapter III has made the reader familiar with this concept; it will here be considered in a more systematic way

Dermatophytids

The "id" or "ide" suffix was originally proposed by Darier to designate certain characteristic skin lesions in tuberculosis and was later applied to other infectious diseases At first, because of inability to recover organisms from these lesions they were thought to be caused solely by non-living microbial products Later work however has shown that the micro-organism itself is in most cases brought to the skin the "id" reaction is probably an allergic

response to the presence of the organism in sensitized tissue This may represent a form of immunity very probably so in view of the rapidity with which the organism is destroyed but the consideration of this question is irrelevant here. Though these lesions are typically the response to living organisms, it is still possible that in some cases they may represent a reaction to microbial products only It is certainly true that eczematous eruptions have been produced repeatedly by applying sterile culture filtrates as patch tests (see Chapter VII)

Although "id eruptions from hyphomycetes had been described previously the eczematous type, secondary to tinea of the feet or other areas of the glabrous skin, was first given prominence by Williams. Since this publication the number of cases of "epidermophytid" has become enormous; it is apparent, in fact, that this diagnosis is made far too frequently in some countries and on quite insufficient grounds. Nevertheless, it can be accepted that eczematous eruptions, not only of the hands, may appear as an id" reaction to active eczematous fungal lesions of the feet or elsewhere. An observation, possibly of practical importance, remains to be stated: in animal experiments it has repeatedly been shown that the site of the "id" eruption may be determined by minimal superficial trauma, such as that produced by shaving. This has some bearing on the clinical manifestations of disseminated eczema which will be discussed later

Bacterids

An obvious step from the proved eczematous id" eruptions of fungous infection is to the bacterid. There has been much difference of opinion here, possibly because of the difficulty of proving the pathogenic or allergenic properties of bacteria normally resident on the skin. The French school has long insisted that the sharply demarcated, scaly patches which Darier called *eczématides* are always microbial in origin. Bloch and Sabouraud also regarded micro-organisms or their toxins as potential allergens and specifically included bacterids among eczematous manifestations. Chapter VII demonstrates how much further this concept has been taken by modern workers.

These bacterid eruptions cannot be distinguished clinically or histologically from other disseminated eczemas; though they may imitate the parent lesion and present only red, sharply demarcated patches, they may readily show as papules or vesicles, grouped or scattered (Fig. 53)

Autosensitization

We have now traced the development of disseminated eczema from systemic spread of fungal bacterial and chemical allergens. The last hypothesis to be considered is the possibility of the skin itself acting as an allergen under certain conditions; Epstein's hypothesis of the development of "protigen" was mentioned in *Chapter III* and becomes relevant again here

The history of early investigation into organ-specific antibodies has been well summarized by Sulzberger[14] modern work dates from the now classical experiment of Burky and Woods.[13] Combining rabbit lens or muscle extracts with staphylococcus toxin and using this mixture as an antigen these workers were able to demonstrate the production of antibodies to lens or muscle in normal rabbits. *In rabbits so prepared minor traumata to the lens or to muscle* then produced local reactions far exceeding those elicited in unprepared control rabbits Omitting many further experiments showing the existence of organ-specific antibodies to brain kidney and hormones, we come to the first demonstration of anti-skin antibody by Hecht Sulzberger and Weil[14] Using rabbits, and substituting rabbit skin extract for lens or muscle, along with staphylococcus toxin these workers were able to demonstrate the formation of precipitins to homologous skin Although the final step of producing cutaneous lesions by minor trauma was not *attempted in this experiment, analogy with much other work makes* it at least probable that positive results will be obtained in this way The new horizon which such studies reveal in the pathogenesis of disseminated eczemas are best summed up in Sulzberger's words[8]

"Is it not possible that damage to the skin (either through infection or through physical agents or through reactions to allergens) may create and liberate skin antigens which in turn produce skin specific antibodies which, in turn produce reactions in the skin itself wherever and when ever skin antigen is made available and accessible to their action? Would not this hypothesis explain—perhaps better than all others—the recog nized fact that after an eczematous response has been produced in one area there often follow months and years during which not only the areas of exposure but also almost all other skin sites, react with pathologic responses to all manner of forces and substances previously innocuous and previously tolerated?"

This postulate that the subject can be primed with antibodies to his own skin and thereafter react with eczematous lesions to the most banal stimuli transports us in a single stride from laboratory to clinic

The word "autosensitization" was coined by Whitfield[11] to explain three different phenomena, of which only one concerns us here. His own words are best used to present his ideas:

> Rubbing of a patch of dry thickened eczema sometimes produces a generalized eruption, at first a punctate erythema but soon becoming a papulo-vesicular eczema.
>
> Again (in) a patch of varicose eczema owing to application of unsuitable treatment there may occur suddenly a generalized eruption all over the base of the neck, the chest and the arms."
>
> "I regard then both of these as instances of extended or generalized eruption, respectively due to the absorption of the patient's own broken down tissue products, and I believe also that this is the mechanism by which an eczema produced by external irritants such as hair dye, etc., extends far beyond the original site of application and often appears in remote parts such as the flexures of the elbows, the inguinal and the submammary regions, etc.

This concept has been enthusiastically supported by many. Milbradt reported finding sensitivity to human skin in certain human beings, and Ingram went so far as to state that autosensitization is an aetiological factor in every case of eczema. Templeton and his co-workers claim to have produced precipitins to skin extract in five volunteers after four injections of this extract; no added bacterial toxin was used. Cormia and Esplin tested patients suffering from "autoeczematization" with skin and other extracts; positive wheal reactions were obtained in many cases, not only to scale extracts, but to blister fluid and leucocyte suspensions. The last suggested to them that autosensitization occurring during X-ray therapy of eczematous areas may be caused by the release of proteolytic enzymes from destroyed leucocytes. Deductions based on this work must necessarily be tentative as only urticarial, and not eczematous reactions were demonstrated. The same objection attaches to the work of Hampton and Cooke,[19] who obtained similar positive tests with human dander extract and demonstrated the presence of passive transfer antibodies. As the reader will recall, this finding is at variance with our concept of non-atopic eczema.

Hopkins and Burky though concerned primarily with eczema of the hands, suggested a sensitization to a combination of the patient's own keratin and staphylococcus toxin. From every point of view this is a reasonable hypothesis, for it at once co-ordinates clinical with laboratory findings. Further it offers an acceptable compromise between the pure bacterid hypothesis and the pure autosensitization concept of Whitfield. At this stage of our

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This postulate, that the subject can be primed with antibodies to his own skin and thereafter react with eczematous lesions to the most banal stimuli transports us in a single stride from laboratory to clinic

synergic effect of bacteria. Such a hypothesis is, of course highly speculative; nevertheless, a comparable observation has been made in experimental animals. Burky[1] recorded that, in rabbits sensitized with *muscle* extract and staphylococcus toxin, minor trauma to the *skin* produced a disproportionate *cutaneous* reaction. Such a finding is of great interest but must not lead us further at this stage, for the direct transfer to humans of conclusions based on the experimental animal is highly fallacious. Endogenous eczema has always offered temptation to the theorizer for its erratic behaviour can be fitted to almost any hypothesis; the reader will therefore find that much of what follows is unproved, debatable and contentious.

Drug Eruptions. Here at least we are on firm ground, for numerous drugs are known to produce an eczematous eruption, both in naked eye appearance and by histological criteria. Such eczemas result from ingestion, injection or other forms of parenteral absorption of the drug, without previous epicutaneous contact. The chief offenders are arsenic, especially when injected as arsphenamine (salvarsan) compounds, mepacrine (atabrine) ephedrine, formalin, iodine, ipecacuanha, mercury penicillin procaine, quinine salicylates and sulphonamides.

The appearances are those of any symmetrical eczema and are usually of acute onset. In general these eruptions obey the basic rules for allergic eczemas set out in Chapter I sensitizing exposure, incubation period and eliciting exposure can always be established when an accurate history is obtained. The phenomenon of spontaneous flare-up may be evidenced by the appearance of the first sign of eczema four or more days after the first and only exhibition of the drug. It may be pedantic to remind the reader that an eczema classified as a drug eruption must be the result solely of internal administration; when the eruption follows the external application of the drug, either in the sensitizing or eliciting exposure, it is classified as a contact eczema. The fact that a patch test with the causative ingested drug is positive need not deter one from regarding the case as one of endogenous eczema, for this phenomenon is commonly found in cases of eczematous drug eruption without previous epicutaneous contact. The patch test is, in fact, a useful diagnostic procedure in these cases and often obviates the potentially dangerous one of administering a suspected drug by mouth.

knowledge we are entitled to believe that *autosensitization to the patient's own skin products is probably a real event and that it can be produced more readily in the presence of bacterial (especially staphylococcal?) infection.* It must, however, be emphasized that this still remains a belief. Although it appears to explain most of the phenomena we observe so frequently, "final proof of the existence of this mechanism in man is still lacking" (Sulzberger and Baer[3].)

Causes of Dissemination. In many cases certain events at the site of a localized eczema are clearly the cause of a generalized outbreak. In most instances some form of irritation has preceded a local flare-up: bacterial infection, the use of unsuitable topical medication, excessive rubbing and scratching, or a combination of these three factors are usually observed. The use of occlusive, particularly greasy applications is the means by which any of these factors is most commonly produced. Local X-ray therapy is also believed to initiate dissemination in some cases, as mentioned previously.

ENDOGENOUS ECZEMA

There remain for consideration a number of cases of symmetrical, more or less generalized eczema in whom no primary cutaneous focus can be demonstrated.* These are the dwindling remnants of the *eczéma-maladie, eczéma vrai* or *eczématose* of the French. It must be stated at the outset that the clinical and histological picture of endogenous or "true"† eczema is non-specific. Bloch remarked, "Experimental sensitization can produce every clinical, macroscopic and microscopic histologic change which is considered characteristic of true eczema." Thus the diagnosis of "true" eczema rests solely on the absence of a demonstrable primary lesion or other cause: it is a diagnosis by exclusion with all its attendant fallacies.

Before considering the various known and assumed causes of this "disease," it should be mentioned that a variant of the sensitization phenomenon is still a possibility. But instead of skin products forming the allergen, we should have to postulate an allergen derived from some other tissue, with or without the

* The possibility of course exists that such patients may have had an eczematous lesion of which they have no recollection, for instance non-atopic [illegible] eczema.

† The word "true" is used in Chapter IV for eczema showing characteristic intra-epidermal vesiculation; here its meaning may be taken as equivalent to "endogenous".

dermatitis may show an eczematous phase, even in adults and especially when affecting the hands, and secondly that in these cases the possibility of contact eczema from handling the suspected foods must always be remembered.

After reviewing much recent work in this subject I feel that instances of non-atopic eczema caused by the ingestion and not the handling of foods are uncommon. They become positively rare when cases suffering from coincident contact eczema or bacterial infection are excluded. Personal experience has been discouraging: of the many cases subjected to rigid elimination diets, some of them under close supervision, few have shown the clear-cut results that one awaits. Of those who recovered after elimination of certain specific foods, a proportion had recurrences within a short time; further dietary testing then revealed that not only could no further foods be incriminated, but that partaking of the previously incriminated foods produced no further deterioration. The foregoing remarks do not imply that the question of diet must be ignored indeed, it may well be found to represent one of a number of aetiological factors and will require investigation and treatment equally with the others.

Infective foci. These have been considered in Chapter VII and need not concern us here. The rôle of *virus infections* in the production of eczemas is uncertain; though a viral causation is often suspected, the only authenticated examples to come to my notice are cited by Sonck.[36] He has seen several hundred patients developing solar dermatitis as the result of infection with the virus of lymphogranuloma inguinale. This complication is commoner in infected women, among whom Sonck found an incidence of 55 per cent. with various types of light sensitivity eruption, compared with 12 per cent. in males.

Dermatitis Herpetiformis. Gordon and Loewenthal[37] have suggested that certain cases of chronic endogenous eczema of unknown causation represent a variety of the Duhring-Brocq disease. It must be admitted that areas of eczema, as judged by clinical and histological criteria, are frequently found along with the more typical bullous lesions of this disease; it is therefore conceivable that these eczematous outbreaks can be the sole manifestation of dermatitis herpetiformis. It is, in fact, not uncommon for a patient to be regarded as a case of endogenous eczema for weeks or months until the more typical manifestations of dermatitis herpetiformis

Eczema from Foods. Here I do not refer to such vague generalizations as "rich foods" or the "high living and low life" of earlier writers An eczema to be considered as caused in this way must be a specific allergic response to certain foods appearing when they are administered and disappearing when they are withheld And in order to be reasonably sure of such dietary origin these administrations and withdrawals should be made without the patient s knowledge. It must also be shown that such cases are of an eczematous and not atopic nature, for the presence of allergic reactions to foods is a commonplace in the latter condition

Until the last decade convincing cases were rarely reported and even in these Miescher[3] *stressed the fact that the patients had handled* the incriminated articles of diet for long periods, thus *suggesting a recrudescence by ingestion of an original contact* eczema In 1946 Flood and Perry[4] detailed thirty cases in whom *a vesicular eczema of the hands disappeared after elimination of* certain presumably allergenic foods, and recurred after their *ingestion later When these results are cited by other authors* an important fact is usually ignored Flood and Perry found "contributory" *factors* such as contact eczema and bacterial *infection* in exactly two thirds of their patients. The unbiassed critic must wonder whether the dietary factor could not, with equal *fairness*, be called contributory to the other conditions At about the same time Rowe reported on eighty patients with *atopic* dermatitis of the hands due to food allergy the quoting of this series along with that of Flood and Perry and without the necessary *qualification* seems theoretically unsound. Livingood and Pillsbury[11] published a further series of twenty-six patients *with eczematous dermatitis* (presumably non-atopic) in whom specific food factors were alleged to be the only causative agent or a *significant contributory cause*. The lesions were not limited to the hands in sixteen of the cases reviewed Again the authors *mention contributory*" *factors* and again the presence of proved contact sensitivity and bacterial infection is noted, *in fact in two of the three cases presented with full* particulars the existence of multiple contact allergens was proved by patch *testing and in the third numerous positive reactions* to scratch tests with foods were obtained Sulzberger in discussion wisely urged *that cases of this nature should be divided into* atopic and non-atopic groups; he gave it as his impression that beneficial results from *food elimination* would be far more frequent in the former He raised two other points of interest first that atopi

and its self-disinfecting power have been considered in Chapter VI. Of the remainder the question of vague metabolites must remain open; today we can say no more than did Bloch[23] over twenty years ago: "there is not the least evidence of the existence of a metabolic disturbance which is common to all or to many types of eczema and which is pathognomonic for this condition of the skin. In only exceptional cases can a specific metabolite such as a *porphyrin*, be demonstrated; in the great majority it is better to confess our ignorance.

Heredity

It is highly unlikely that a predisposition to eczema can be inherited or transmitted in the human. By selective breeding in animals, on the other hand, it is possible to obtain strains which can, or cannot be sensitized easily by artificial means.[24]

Race

Comparative studies are quite inadequate for us to be dogmatic about racial predisposition It is usually believed that the Negro races are relatively immune from contact eczema, but real evidence on this point is lacking.

Type of Skin

It is probable that persons with blond colouring and relatively dry skin are more susceptible to external noxae; certain aspects of this problem have been dealt with in Chapter VI

Geographical Factors

Climatic effects may depend to a great extent on alterations in sweating and the growth of surface bacteria under various conditions of heat and humidity Beneficial results often follow a change to a dry climate at higher altitude in many types of eczema, it is less generally known that patients developing eczemas in these high dry climates may show equal improvement from a change to sea level These observations, however have no bearing on the aetiology of the eczemas, which apparently occur with equal readiness in all parts of the world. This is not necessarily so in experimental animals, as was shown by Sulzberger and Mayer

Nutritional Factors

The cutaneous signs of *pellagra* may be those of an eczematous reaction to sunlight.

appear (*see* Fig 54) Many other features, eosinophilia the distribution intolerance to iodides and bromides, residual pigmentation and response to certain forms of treatment are common to the two diseases and offer no certain means of differential diagnosis.



FIG. 54
Papulo-vesicular form of dermatitis herpetiformis. These eczematous lesions were the only form of the disease for a period of six months.

Malignant Reticuloses (Lymphoblastoma) Rarely an endogenous eczema may be the first sign of these conditions especially of mycosis fungoides. As a rule such eruptions are preceded by *pruritus of long duration and attention is directed to the underlying* cause by the bizarre configuration of the eczematous areas, or by the co-existence of morphologically distinct lesions such as urticaria

PREDISPOSING FACTORS IN NON ATOPIC ECZEMA

It was mentioned earlier that a fundamental problem common to many fields of Medicine, lies in the question "what makes this patient, out of all the persons with equal opportunity contract this particular morbid condition?" The question of personal idiosyncrasy has so far not been solved and in non-atopic eczema it has given rise to much speculation It is my purpose here to examine briefly some of the alleged predisposing causes two of the most *important, that is the skin s capacity to neutralize acids and alkalis*

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originating during pregnancy may be caused solely by the gravid state. Their possible relationship with dermatitis herpetiformis and herpes gestationis may be considered.

Fluctuations in chronic eczemas frequently coincide with certain phases of the menstrual cycle and this phenomenon may be so marked as to suggest the diagnosis of " menstrual " or " dysmenorrhoeic " dermatitis. It is probable, however that the endocrine,



FIG. 55
The Koebner Phenomenon in chronic endogenous eczema. Fresh lesions have appeared along scratch marks.

chemical and allergic variations observed during the cycle are only contributory and it is usually impossible to incriminate any single factor regular fluctuations in the surface pH, as described by *Blank*,[44] could represent the mechanism by which such changes are brought about.

EFFECTS OF NON-SPECIFIC TRAUMA

The Koebner Isomorphic Reaction consists of the production by non-specific irritation, of lesions identical with the clinical dermatosis. Thus, in lichen planus, scratching of the skin may produce lesions of lichen planus at the site of injury In eczema various types of trauma will, in some cases, produce eczematous lesions at the traumatized site (Fig. 55) Attention was drawn to this phenomenon in considering "id" eruptions earlier in this chapter An interesting example is illustrated in Figure 56, this subject of disseminated eczema produced lesions on all pressure areas, highly

Seborrhoeic and *endogenous* eczema have been found in association with macrocytic anaemia and with evidence of disturbed liver function. Ayres *et al* have recently summarized previous work and have confirmed that many middle aged and elderly patients with eczema are relieved or cured by injections of crude liver extract and vitamins by mouth. Cerny [3] in fact, found that the great majority of cases of "eczema and dermatitis," when subjected to a battery of tests for liver function, showed evidence of disturbed hepatic function.

The mechanism by which eczema can be caused in this way has not been elucidated, one may suspect a failure to detoxicate endogenous products but with this, as with other nebulous hypotheses, further investigation is obviously required The same may be said of claims that eczema can be relieved or cured by the administration of essential unsaturated fatty acids, so-called Vitamin F or of biotin in infantile cases A point of some interest which I can personally confirm is that eczemas are not more commonly encountered in chronically malnourished populations, with the exception of certain seborrhoeic eruptions as described for instance by Simons [34]

Endocrine Influences

Involutional changes may account for certain cases seen in the fifth and later decades of life. It would seem probable that they act by altering the architecture and secretory mechanisms of the skin It must be remembered however that eczema is not a recognized presenting sign in any of the known syndromes of endocrine imbalance, nor is it a manifestation of overdosage with any endocrine preparation

The effects of pregnancy offer an intriguing problem, for eczema in common with many other diseases, may show remarkable variations at this time. As an example I may quote two cases of contact eczema

The first was sensitive to *nasturtium hollyhock and verbena* the sensitivity appeared during a pregnancy when the foetus had died *in utero* and persisted for four years, except *during the last seven months* of two subsequent, successful pregnancies. The second was sensitive to nickel, but this sensitivity appeared only *during the latter half of* three successive pregnancies at other times the skin was clear and patch tests were negative

These cases illustrate that pregnancy may act as a contributory factor it is not known whether any of the eczemas frequently

is the principal factor in the production of eczema to the ultra conservative view that such influences are infrequent and of negligible importance. An adequate bibliography would alone exceed the limits of space which have to be set; perhaps the most satisfactory solution is to refer the enquirer to a recent contribution* in which useful references are given for literary research. It is recommended, in reading, that the heady draughts of psychosomatic enthusiasts be taken with small doses of a sobering kind, such as Sulzberger and Baer's review For over-enthusiasm has undoubtedly done the study of this problem more harm than has mere opposition. As Stokes and Beerman say: "The lack of objective mensuration, the paucity of experimental studies under anything like adequate controls, the fact that there exists no adequate study of normals for base-line comparative purposes and that much of the pathological material reported has too much of an I had a case quality all impede investigation and discredit conclusions." On the other hand, scepticism on general principles is also to be deplored and the critic must free his mind of prejudice. As the same authors remark. "The very word psychic carries dubious implications of charlatanism and art-magic of which we must certainly rid ourselves if real progress is to be made."

The reciprocal effects of mind and body require further exploration. That they exist cannot be denied; their degree must vary from case to case and an assessment of their relative importance is surely one of the duties of the dermatologist. Another duty rarely mentioned, is the prevention or alleviation of psychic trauma caused by skin disease; this should often be within our powers, if we are to regard ourselves as medical men and not simply specialists in one organ.

My personal views on psychogenic eczema are of little importance. I have found it easy to deride the over-enthusiastic* and difficult to ignore the many suggestive incidents encountered every day Nevertheless, I believe that a psychosomatic explanation of aetiology in the present state of our knowledge, must be subject to certain conditions: it should be the last factor considered, not the first; it should not be adduced simply through lack of a somatic explanation, that is by exclusion; and it should not be employed, in desperation, as an unconscious means of shifting the blame from our own inadequacy to the patient's temperament. The last, a failing common to us all may be good psychotherapy—but only for the doctor Among the commoner fallacies are the tendency to ascribe

reminiscent of contact eczema from a lavatory seat when it appeared on the buttocks.

Not only can non specific trauma initiate fresh lesions but it can and does frequently *prevent the natural recovery of existing ones.* This may often be clearly demonstrated by occluding a portion of the eruption with a zinc-gelatine bandage and observing the acceler ated rate of recovery in the protected area It may be significant that the majority of lesions in disseminated eczemas are in those

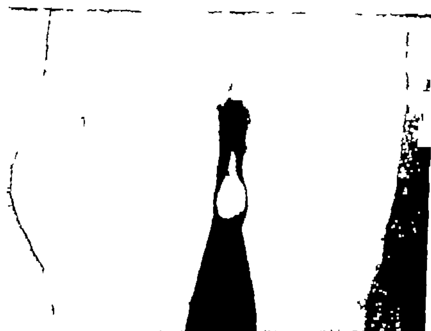


Fig. 56
Lesions produced by the pressure of sitting (Koebner Phenomenon). V f contact eczema from a lavatory seat

areas most accessible to the finger nails it is surely permissible to believe that scratching has either determined the localization of much of the eruption or its chronicity

Parasitic Infestations

Stauffer has recently drawn attention to the rôle of *Ascaris* in producing maintaining or aggravating various dermatoses Among these were cases of different types of eczema and anti-ascaris treat ment was in many instances beneficial to the skin

Nervous and Emotional Factors

For various reasons it is impossible to do justice to this huge, hotly debated and uncertain problem Opinion among dermatologists ranges from the conviction that a psychosomatic mechanism

is the principal factor in the production of eczema to the ultra conservative view that such influences are infrequent and of negligible importance. An adequate bibliography would alone exceed the limits of space which have to be set; perhaps the most satisfactory solution is to refer the enquirer to a recent contribution[11] in which useful references are given for literary research. It is recommended, in reading, that the heady draughts of psychosomatic enthusiasts be taken with small doses of a sobering kind, such as Sulzberger and Baer's review. For over-enthusiasm has undoubtedly done the study of this problem more harm than has mere opposition. As Stokes and Beerman say: "The lack of objective mensuration, the paucity of experimental studies under anything like adequate controls, the fact that there exists no adequate study of normals for base-line comparative purposes and that much of the pathological material reported has too much of an 'I had a case' quality all impede investigation and discredit conclusions. On the other hand, scepticism on general principles is also to be deplored and the critic must free his mind of prejudice. As the same authors remark: "The very word 'psychic' carries dubious implications of charlatanism and art-magic, of which we must certainly rid ourselves if real progress is to be made."

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skin diseases to emotional causes without satisfying the essential criteria *of proof demanded* of every scientist' disregard of the natural course and fluctuations of many skin diseases; and accepting a cure by psychotherapy as proof of psychogenic causation Another disservice done to the unbiassed study of psychosomatic mechanisms is the attempt to link certain skin diseases with certain types of personality such as obsessional and hysterical ' This has led to repeated and profound differences between investigators and tempts one, quite illogically *to view the whole subject with suspicion. The* last fallacy to be mentioned is the psychosomatic bias derived from the word "neurodermatitis, used in a sense quite differ-nt from Brocq s original and unprecise concept. '

In this discussion I shall limit myself to the consideration of known and generally acknowledged phenomena which may act, in different kinds of eczema as *contributory or aggravating factors*

Physiological Changes. *It is common knowledge that flushing* and blanching even in normal subjects, are frequently of emotional origin *An ingenious experiment by Kepecs, Robin and Brunner'* shows that exudation from an artificial blister site increases with the shedding of tears; the common use of the adjective "weeping" for certain eczemas will undoubtedly be of significance to the psychologist but only in respect of English-speaking patients Here, then, are two mechanisms, flushing and exudation by which emotional factors may aggravate a pre-existing eczema A third factor equally common in emotional states, is sweating Its effect on the chemistry of the skin surface, and consequently on eczema *have been considered in Chapter VI A further* aspect ably presented by Sulzberger is the possibility of itching attacks being produced by an attempt to sweat when *the ducts are plugged* by some morbid process, such as certain of the eczemas. The fourth mechanism is through cholinergic and possibly adrenergic effects in the former not only sweating, but flushing and dermal exudation of serum have to be taken into account. It has even been suggested that muscular tenseness may produce cutaneous effects by liberation of excessive acetylcholine

It will be noticed that all the foregoing hypotheses are BASED ON PHYSIOLOGICAL GROUNDS capable of experimental verification

Personality Factors. *Hall Smith and Norton surprised at th* high proportion of psy-hically abnormal people with non-psychogenic skin complaints *such as pityriasis rosea and scabies* suggested that such people are constitutionally "fussy" Among th-m will

be found the querulous, the self-medicators and the scratchers. It is these who will drift most readily to the hospital, and as most series are drawn from hospital populations these people will naturally cause errors of selection. In considering the eczemas these aberrations of personality may well be of great contributory importance, for scratching and self-medication are two common ways of perpetuating and spreading eczematous eruptions. Similarly individual variations in the itch threshold may account for some apparent paradoxes in the study of eczema

In short, then an abnormal psyche may aggravate or perpetuate any eczema through the production of a Koebner phenomenon or by infection, both mediated by excessive rubbing and scratching; through abnormal vascular responses, leading to increased itching and exudation; and finally through an affection of the sweat mechanism, either by obstruction of the glands or by the production of an abnormal sweat and consequent disturbance of the superficial acid-base equilibrium. These mechanisms should surely suffice to explain many examples of psychosomatic effects in eczema without having to postulate a primary and direct psychogenic eczema, for which adequate proof is so far lacking.

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CHAPTER X

ECZEMATOUS ERUPTIONS WITH SPECIAL FEATURES

S GORDON

IN this chapter a number of eczematous eruptions are selected for detailed discussion either because they illustrate known facts with particular clarity or because they present difficulties of integration within the framework of an aetiological classification of eczema. Thus hand eczema was selected because of the innate difficulty of differentiation between the various types of eczema when the hands alone are affected. Hypostatic eczema or congestive eczema, offers no such diagnostic difficulty but a clear understanding of the mechanism underlying the production of the eczema reaction is necessary for effective treatment. Eczema of infancy is introduced because it is felt that its complete identification with atopic eczema, as is usually done, is an over-simplification, which ignores the possibility that other forms of eczema may occur in infants.

NUMMULAR ECZEMA

Description. Nummular eczema is a survivor from the days of purely descriptive dermatology when papules, vesicles, scales, or crusts determined the status of an eczematous rash. At present it has a tenuous existence on the strength of a very distinctive morphology As the name denotes, the lesions are discrete and coin-shaped. They are erythematous plaques studded with small vesicles or papules. Oozing from the pits of ruptured vesicles leads to the formation of crusts These lesions may be exudative in the acute stage and become scaly in the more chronic phase. There is a uniformity of shape about these coin-like lesions, but considerable differences in size are not uncommon. The large lesions seem to develop as discoid plaques which extend by confluence with satellite lesions at the periphery Very often the condition clears up with

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treatment, but recurrences are frequent and these will manifest themselves by the re-appearance of papules and vesicles on the residual erythema of a pre-existing plaque. (*See* Figs. 7 to 11 Chapter I)



FIG. 57
Asteatotic, fissured skin—early case

The distribution of the lesions is fairly constant The dorsa of the hands and fingers, the extensor surfaces of the limbs, the dorsa of the feet and the shoulders are the sites of involvement in that order of frequency Itching is a variable symptom but is usually present in some degree. In some cases it is severe throughout the course, in others it is marked at the outbreak of new lesions and then subsides. In many cases nummular eczema appears and re-appears in the cold season and remits in summer

Causation. The above is the common clinical picture with which every dermatologist is familiar Unfortunately the aetiological significance of this picture means many things to many people Gross associated nummular eczema with asteatosis asteatotic eczema or bath dermatitis The asteatotic skin is dry slightly scaly erythematous and shows very superficial fissuring on the surface This is most marked on the legs and gives the appearance of a crazy paving pattern (Figs. 57 and 58) The condition is worse in winter and is aggravated by cold wind dry spells bathing and



FIG. 58
Asteatotic, fissured skin—advanced case.

alkalis It is commoner in the elderly Gross attaches significance to the frequent association of nummular eczema and a dry skin (Fig. 59) He finds that the distribution the occurrence in winter and the aggravating effect of soap and water are features common to nummular eczema and asteatosis and on the basis of this similarity he assumes that asteatosis is a predisposing factor in nummular eczema He considers the possibility that the unfavourable effect of the cold season on both conditions is due to the lowered



FIG. 59
Nummular pattern developing on asteatotic skin. Onset in winter

Vitamin A content of winter food and reports good response to treatment with Vitamin A In his series the use of soap and water was discouraged while active lesions were present and a bland ointment was used. Gross attaches very little importance to these adjuvant measures, but his argument is not convincing Another question raised by Gross is whether "dermatitis of the hands in housewives" is not also a form of nummular eczema resulting from the excessive use of soap and other alkalis.

In the discussion of Gross's paper divergent views were expressed S W Becker argued against a definite relationship between nummular eczema and asteatosis He associated asteatosis with "winter eczema" and classed nummular eczema as one form of exudative neurodermatitis of Kreibich Becker offered the hypothesis that nummular eczema results from retrograd nerve impulses with production of irritating chemicals in the skin" (what ever that may mean) E. C Fox argued in favour of a bacterial aetiology Unfortunately for his argument his claim for the efficacy

of sulphanilamide therapy has not stood the test of time, but some cases of nummular eczema certainly respond rapidly to topical anti bacterial applications. J G Downing expressed the opinion that nummular eczema has a different aetiology in different classes of patients. H. Niles suggested that the condition may be due to a virus infection, or that it may be a variant of dermatitis herpetiformis.

This discussion, although it lists quite a number of conditions in which the nummular eczema pattern may be the presenting feature does not by any means exhaust the possibilities. Gross draws a sharp distinction between the clinical appearance of a nummular eczema and that of a contact dermatitis. On the whole this distinction is clear-cut when a nummular eczematous patch is compared to an eczematous rash at the point of actual exposure to a contactant, but when an eczema disseminates from a focus of contact sensitization, the general rash may have all the features of a nummular eczema. Even the distribution may be that commonly encountered in a nummular eczema which appears to have arisen idiopathically Van Studdiford *et al*[7] believe that the condition is associated with diminished gonadal function. Carpenter *et al*[8] produce evidence in support of a relationship between focal sepsis and nummular eczema. The eczematous type of drug eruption as seen with quinine, sulpha drugs, mercury and the halogens will occasionally appear in the guise of a nummular eczema Rowe described a nummular eczematous pattern in some of his cases of eczema of the hands which he attributed to food allergy

It would seem then that no case can be made out for the view that nummular eczema is a single and distinct entity In view of what has been said (Chapters I and XI) about the diagnosis by morphe it would be desirable at this stage to use the term nummular eczema with the reservation that it conveys no meaning other than the description of a familiar clinical picture.

ECZEMA OF THE HANDS

Cheiropompholyx. Eczema reactions of the hands have confronted the dermatologist with some of his most perplexing problems. It may almost be said that the more experience a dermatologist has gained the more aware he becomes of the difficulty in determining the nature of an eczema reaction on the hands. The mere fact that the term cheiropompholyx came into being in an attempt to unify the vesicular eczema eruptions of the hands bears

testimony to a curious misinterpretation of a physical sign and indicates that the morphology of such an eczema reaction affords no clue to its aetiology For a time it was thought that the term was synonymous with dyshidrosis and that the vesicles represented dilated sweat ducts [1] It seems incredible that generations of dermatologists failed to make the self-evident observation that if a person is sensitized to something he handles, he may develop a pompholyx eruption of the hands. If he then touches his face while a residue of the sensitizing substance is still present on his fingers he develops another type of eczema reaction on the face. Cheiropompholyx incidentally is a very unfortunate term Such a distinguished representative of medical nosology could not fail to acquire a more important meaning than the term was intended to convey

Another obvious and highly unsuccessful attempt at simplification was the over-emphasis on the relationship between vesicles of the hands and any maceration or fissuring between the toes to which the label "fungus" could be attached If we now accept that owing to the anatomical features of the hand any eczema whether of endogenous or exogenous nature, may manifest itself as a vesicular sago grain" eruption it becomes obvious that no unification of aetiology is possible and no panacea is likely to be of assistance in therapy

There is no constant relationship between the aetiological basis of an eczema of the hand and the morphological form it might assume. The eczema reaction whether endogenous or exogenous, chemical or bacterial may appear in its most acute form with enormous oedema of the hands and large bullae, to be followed by glove-like shedding of the skin In a milder reaction the eruption may be in the form of deep-seated vesicles—the so-called "sago grains" Patchy eczema may be papulo-vesicular scaly crusted fissured or superficially denuded with undermined edges. Very often one can see sago grains on the fingers and discoid patches on the dorsum of the hand in the same attack

Id eruptions An active fungus infection of the feet will often give rise to a vesicular eczema of the hands, this being, perhaps the most typical example of an "id eruption but the identical eczema reaction could be secondary to a bacterial infection of the feet, or sensitization to shoe leather (Fig 60) or topical medicaments Moreover if the sensitizing agent acts directly on the hands it can produce a reaction which is indistinguishable from the "id" eruption There is a fine distinction between a fungal

id" and an eczema of the hands secondary to bacterial or chemical sensitization of the feet. Whereas in the latter an eczema reaction of the feet precedes the eczema of the hands, with dermatophytosis it is often found that an eczema reaction of the hands appears without any preceding eczema of the feet, in the usually accepted sense. Even this distinction falls away if one is prepared to regard the vesicles and inflammatory fissures of a dermatophytosis as a form of eczematous reaction to a fungal allergen.



Fig 60
Nummular eczematous eruption of hand, secondary to contact eczema of the feet from shoe leather

Contact Eczema. The reaction of the skin of the hands to a contact allergen can produce any morphological type of eczema. Reactions to liquids, greases, dusts, or plants will generally produce a diffuse symmetrical eruption, whereas contact with solids produces localized patches, which affect one hand only or one hand more than the other The usual pattern may however be altered by several factors, *e.g* the degree of sensitivity the amount of sweating, the mode and frequency of contact, secondary irritation by soap and water and the medicaments applied. As would be expected, contact sensitivity is a major factor in the aetiology of hand eczema, the percentage in any particular series depending on the skill and

testimony to a curious misinterpretation of a physical sign and indicates that the morphology of such an eczema reaction affords no clue to its aetiology For a time it was thought that the term was synonymous with dyshidrosis and that the vesicles represented dilated sweat ducts[4] It seems incredible that generations of dermatologists failed to make the self-evident observation that, if a person is sensitized to something he handles he may develop a pompholyx eruption of the hands. If he then touches his face while a residue of the sensitizing substance is still present on his fingers he develops another type of eczema reaction on the face. Cheiropompholyx, incidentally is a very unfortunate term Such a distinguished representative of medical nosology could not fail to acquire a more important meaning than the term was intended to convey

Another obvious and highly unsuccessful attempt at simplification was the over-emphasis on the relationship between vesicles of the hands and any maceration or fissuring between the toes to which the label " fungus could be attached If we now accept that owing to the anatomical features of the hand any eczema whether of endogenous or exogenous nature, may manifest itself as a vesicular " sago grain " eruption it becomes obvious that no unification of aetiology is possible and no panacea is likely to be of assistance in therapy

There is no constant relationship between the aetiological basis of an eczema of the hand and the morphological form it might assume. The eczema reaction whether endogenous or exogenous, chemical or bacterial may appear in its most acute form with enormous oedema of the hands and large bullae, to be followed by glove-like shedding of the skin In a milder reaction the eruption may be in the form of deep-seated vesicles—the so-called " sago grains." Patchy eczema may be papulo-vesicular scaly crusted, fissured or superficially denuded with undermined edges. Very often one can see sago grains on the fingers and discoid patches on the dorsum of the hand in the same attack

Id eruptions An active fungus infection of the feet will often give rise to a vesicular eczema of the hands this being, perhaps, the most typical example of an " id " eruption but the identical eczema reaction could b secondary to a bacterial infection of the feet or sensitization to shoe leather (Fig 60) or topical medicaments. Moreover if the sensitizing agent acts directly on the hands it can produce a reaction which is indistinguishabl from the id " eruption There is a fine distinction between a fungal

"id and an eczema of the hands secondary to bacterial or chemical sensitization of the feet. Whereas in the latter an eczema reaction of the feet precedes the eczema of the hands, with dermatophytosis it is often found that an eczema reaction of the hands appears without any preceding eczema of the feet, in the usually accepted sense. Even this distinction falls away if one is prepared to regard the vesicles and inflammatory fissures of a dermatophytosis as a form of eczematous reaction to a fungal allergen.



FIG 60
Nummular eczematous eruption of hand, secondary t contact eczema of the feet from shoe leather

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FIG 60
Nummular eczematous eruption of hand, secondary to contact eczema of the feet from shoe leather

Contact Eczema. The reaction of the skin of the hands to a contact allergen can produce any *morphological type of eczema.* Reactions to liquids, greases, dusts, or plants will generally produce a diffuse symmetrical eruption, whereas contact with solids produces localized patches, which affect one hand only or one hand more than the other The usual pattern may however be altered by several factors, *e.g* the degree of sensitivity the amount of sweating, the mode and frequency of contact, secondary irritation by soap and water and the medicaments applied As would be expected, contact sensitivity is a major factor in the aetiology of hand eczema, the percentage in any particular series depending on the skill and

energy with which the search for the contactant is pursued. Waldbott and O Shea[7] have drawn such a formidable list of possible contactants, in relation to hand eczema that certainty in diagnosis seems impossible without exhaustive investigation and prolonged observation of the patient Their attempt to draw patterns of hand eczema as a key to diagnosis seems to have little practical application



FIG. 61
Atopic dermatitis. Only the hands were affected at the time this photograph was taken.

Food Allergy On the other hand, a number of papers claiming an endogenous origin *i e* food allergy for a high percentage of *hand eczemas have appeared in recent years. The editors of the* Yearbook of Dermatology in a review of these papers, state: "If foods have anything like the importance in hand eruptions ascribed to them by these authors, then dermatologists have for many years overlooked an important factor in these resistant and difficult eruptions" "Despite intensified efforts in the last few years we have seen only a few cases in which there appeared to be proof or at least strong suggestion *that foods were causal agents*" We are obviously not yet in a position to state what percentage of cases of hand eczema are permanently cured by food elimination alon and this is, after all the ultimate criterion It will be noted that in none of these papers on exog nous or endogenous hand eczema

was it claimed that a selection of cases for investigation was made on the basis of some morphological picture which is peculiar to the group As stated in Chapter IX, atopic dermatitis may affect the hands only in which case aggravation by foods would be understandable (Fig. 61)

While the association between food allergens and hand eczema is not as clear-cut as we would like it to be, there is no question



FIG. 62
Pompholyx eruption caused by iodine administered for pyelography Only the hands and feet were affected.

at all about the specificity of certain eczema reactions of the hands appearing after the ingestion of drugs. Quinine, salicylates, and the sulphonamides are in particular noted for their relationship to vesicular eczematous eruptions of the hands, which clear immediately when the drug is withheld (Fig. 62)

The familiar pattern of nummular eczema is frequently seen on the back of the hands. When it occurs as part of a generalized nummular eczema, it offers no particular problem by virtue of its localization, but when it is limited to the hands its shape or form has no particular significance and requires the same approach as any other type of eczema.

Infective Eczema. The common form of infective eczema of the hands is a discoid papulo-vesicular or scaly plaque which spreads peripherally with a sharp often undermined, edge (Fig. 63) but here again a high degree of sensitivity to the organism may produce a more acute and diffuse eruption. Moreover as the

bacterial eczema is commonly post-traumatic in nature, it follows that the type of trauma will determine the pattern of the eczema reaction. In this connection the part played by soap and other alkalis is of some importance. The so-called "housewife's dermatitis" can so often be cured by the use of a soap substitute that a direct relationship between this form of eczema and alkaline trauma seems to be definitely established. Whether soap acts as a degreaser

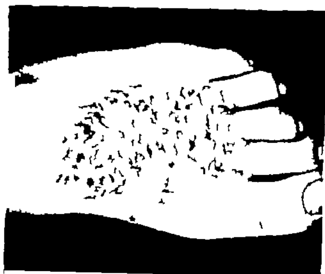


FIG. 63
Bacterial eczema of the foot.

or by its effect on the acid mantle of the skin, or by its caustic effect when the skin lacks the ability to neutralize alkalis is still a matter for speculation. Any one of these effects would explain how a bacterial infection could become superimposed and this is indeed frequently the case (see Chapter VI). The effect of soap in aggravating or perpetuating any other form of hand eczema is probably even more important. While the hydrophobia associated with skin conditions in general is hardly justified in most cases the damaging effect of soap and water on an eczematous skin is a very real hazard. Washing with non-alkaline detergents, e.g., Cetavlon (I.C.I.) or pHisoderm (Winthrop-Stearns) is often not only tolerated but is a useful adjunct to therapy.

Hyperhidrosis. The effect of excessive sweating on hand eczema is nowadays treated with justifiable scepticism. The theory of a direct relationship between hyperhidrosis and pompholyx has been largely discarded, but in view of the work of Shelley and Horvath on artificially induced Milliaria rubra it would seem that the

possibility of sweat obstruction by astringents, fat solvents, and maceration cannot be completely ignored. It has already been mentioned that a sweaty hand is more easily sensitized by contact allergens presumably because the moisture induces more intimate contact with the allergen. It is also conceivable that the skin macerated by sweat is more easily traumatized and that excessive sweating lowers the effectiveness of the acid mantle and predisposes to infection.



FIG. 64
Patch of lichen simplex chronicus on dorsum of hand.

One cannot leave this subject without some mention of psychosomatic factors which have had such a vogue for many years in discussions on cheiropompholyx. It is freely admitted that patches of lichen simplex are common on the hands (Fig. 64) and these are justifiably regarded as psychogenic, but apart from this a psychogenic diagnosis of hand eczema could hardly be made with any degree of confidence, if it is appreciated how easy it is for some endogenous or exogenous factor to remain undetected.

It will be seen that hand eczema is a very complex and difficult subject in which all the problems of eczema have their counterpart and in which the morphe is of very little assistance in making a diagnosis. In practice this amounts to two alternatives: either each case is regarded as a major investigative problem or every diagnosis is regarded as tentative only and liable to early revision if the result of treatment is not satisfactory

NON ATOPIC INFANTILE ECZEMA

Eczema in Infants. *If it were possible to make an unequivocal* statement that infantile eczema is a manifestation of eczema in infancy the whole subject could be disposed of without adding to the burden of the dermatologist or paediatrician Unfortunately such an approach is not possible as long as infantile eczema is still largely identified with atopy Such identification would be justified if by definition the name infantile eczema were limited to atopic eczema *or if evidence were available to show that infants are* immune to other eczematous processes Vickers[1] finds that contact *sensitivity is extremely uncommon before* puberty This is in accord with the general experience that, whereas in adults localized eczema is so often disseminated by injudicious therapy an infantile eczema will remain localized to the face even though it is markedly aggravated by unsuitable applications Percival[1] describes infantile eczema as a single symptom-complex, but states that infective flexural eczema follicular infective eczema and chemical contact *eczema do occur in infants but are rare and can be differentiated* from true infantile eczema by the distribution clinical appearance, *history and course. Peck and Salomon*[3] *after investigating a small* series of cases, conclude that eczema of infants and children does not differ aetiologically from that of adults Hill's division of infantile eczema into dermatitis seborrhoeica true eczema and erythroderma desquamativum shows an awareness of distinct types of infantile eczema, but the term seborrhoeic dermatitis may be said to have outgrown its usefulness and when applied to infants *seems singularly inappropriate Since the work of Martin-Scott* has shown that the *Pityrosporon ovale* is a non-pathogenic saprophyte *seborrhoeic dermatitis has no claim to a separate existence* by virtue of a specific causal organism and the presence of a greasy seborrhoeic state in an infant is hardly conceivable. The use of the expression " true eczema " also calls for some comment Surely a chemical eczema or a bacterial eczema is no less " true than an eczema of unknown causation

While chemical eczema offers no scope for further discussion under this heading, *the question of infective eczema in infants* merits greater attention than it has hitherto received A purely clinical evaluation of the symptoms of infantile eczema shows—and this is particularly obvious in South Africa —that the mode of onset and course of this disease follows two distinct patterns In

√one the condition starts in the early weeks of life as an ill-defined papulo-vesicular symmetrical eczema of the cheeks, which is intensely itchy from the outset. It shows marked excoriation but secondary impetigo is apparently not a pronounced feature, as even in the presence of marked crusting the application of anti bacterial remedies produces only slight improvement. The eruption



FIG. 65
Patch of impetigo at ear This preceded the eczema of the cheeks.

may remain localized to the face, or become more extensive and involve the neck, antecubital fossae, popliteal spaces, wrists and ankles. In these areas it is often rapidly lichenified The disease is obstinate from the outset, extremely resistant to treatment and liable to be perpetuated as a Besnier s Prurigo. If the picture of a Besnier s Prurigo does not develop the condition either clears completely within the first few years of life or leaves a recurrent eczematous patch in one or other of the sites of election of atopic eczema. This type conforms with the usual description of atopic infantile eczema and has been dealt with in Chapter IV

Infective Eczema. Another type of eczema in infants usually also starts in early infancy but may appear between the sixth and twelfth months. The first manifestation may be a "cradle cap," or an asymmetrical crusted, scaly or pustular patch of the face,

ultimately cleared or when the child is older that the underlying papular and lichenified eruption of atopic eczema becomes obvious. In other cases the condition starts very much as described here, but proves much more resistant to treatment and after a time shows involvement of the "atopic areas" with the development of a dry papular eruption A fair assumption is that these cases are primarily infective, but that a latent atopic state is brought to the surface by the infective eczema

HYPOSTATIC OR VARICOSE ECZEMA

Mechanism of Production. As the explanation of the mechanism underlying this type of eczema here offered is based on the views of Anning[14] a better name would be congestive eczema but the old names are retained in order to keep in line with current usage Hypostatic eczema may present itself in one of several forms depending on the ultimate precipitating factor but the underlying mechanism of causation applies with slight variations to all types The vascular system of the lower limb should not be regarded as a large U tube into which blood is introduced at one end by the pumping action of the heart and flows out in equal amounts at the other end from the vena cava into the right side of the heart. The human U tube does not have rigid or impermeable walls and there are loops across the tube joining the two sides. The venous pressure in the feet, when the person is standing at attention, is about equal to the weight of a column of blood extending from the point of measurement to the heart with the addition of the capillary pressure present in the prone position but many factors affect the venous pressure. To maintain a satisfactory return of blood from the legs in the erect posture relay pumping is necessary This is done by the squeezing action of the calf muscles with the assistance of the valves in the veins, which prevent a reflux when the muscles relax.

Failure of the leg muscle pump may result from venous thrombosis, incompetence of deep valves, and lack of muscular action Thrombosis may start in the veins of the foot or the calf and spread upwards into the deep veins. It is more likely to develop in people with varicose veins or when the blood flow in the leg veins is slowed by confinement to bed or in conditions in which the veins are injured or when there is local infection Because of the obstruction in the deep veins an increased flow takes place through the superficial veins which become dilated and varicose The valves of the deep veins may be congenitally absent or they may become

incompetent as a result of dilatation of the veins. The varicosity of the veins may be a familial hereditary abnormality which is aggravated by raised intra-abdominal pressure such as occurs at work which entails standing for long periods, and during pregnancy Destruction of the valves follows thrombosis and recanalisation of the vein produces an irregular valveless tube. With long standing in one position, or with arthritis, contraction of the calf muscles may be too weak or intermittent to act as a pump If the venous return from the limb is defective the result will be oedema, pig mentation, induration, and ulceration. These changes take place as a result of increased venous and capillary pressure with consequent capillary damage and loss of fluid containing protein and red cells into the subcutaneous tissue.

Clinical Appearance. This then is the mechanism underlying the development of varicose veins. The appearance of eczema on the leg so affected could almost be said to be accidental. *In the absence of a defective venous return even pronounced varicosity of the superficial veins is not incompatible with a healthy skin* It is important to bear this in mind in order to avoid the common error of attributing any eczematous eruption of the legs to stasis on the evidence of varicosities only When the venous return is deficient the skin of the lower half of the leg becomes bluish, glazed, shiny and oedematous. If the accumulation of fluid in the subcutaneous tissue becomes organized, the skin becomes adherent to the underlying tissues and loses all elasticity Presence of capillary damage is shown by numerous reddish puncta (Fig. 67) Pigmentation is caused by deposits of haemosiderin. Itching is a marked feature of this state and may be attributed to deficient nutrition of the skin, or to the presence of haemosiderin which acts as a foreign body or to the accumulation of waste products which result from the impaired metabolic exchange in the damaged capillary bed. It is possible that many cases of peri-anal eczema associated with haemorrhoids are essentially of similar aetiology and that their course is also influenced by the erect posture and the indiscriminate use of topical remedies.

The actual development of eczema comes about in several ways. The first change in the skin may be an ulcer which is directly attributable to capillary damage and is precipitated by trauma. Once an ulcer has formed it is possible for the infection to spread peripherally from the ulcer to the surface of the surrounding skin in the same way as it does from any other traumatic or infective

ulcer (Fig 68) The eczema reaction would have the features of an infective eczema It may be limited to the area of devitalized skin but need not necessarily be so It is not unusual to see a large sheet



FIG. 67
First stage of hypostatic eczema, beh nd nd below medial malleolus.

of eczema round the ulcer with discoid sharply defined lesions well beyond its edge on the leg and even the thigh The result of treat ment will often indicate the nature of this eczema as the application of suitable antiseptic applications will improve the eczema sur

rounding the ulcer to some extent, and the outlying lesions to a much greater extent. Even in the absence of an ulcer this infective eczema can appear as a result of introduction of organisms into the skin by scratching. It may take the form of a sharply marginated, erythematous, slightly crusted sheet, or a scaly psoriasiform patch, or a follicular eruption In its most acute form it becomes a large, bright red sheet—eczema rubrum.

Another form of eczema that commonly occurs in such cases is a chemical eczema precipitated by applications to relieve itching or as ulcer dressings. Needless to say combinations of ulceration,



FIG. 64
Infective eczema arising from varicose ulcer

infective eczema, and chemical eczema are quite common. In some cases in the absence of infection, but with much oedema of the subcutaneous tissue, the whole skin of the lower half of the leg becomes thickened, hard and rugose. In such cases there is probably some deficiency of lymph drainage as a result of repeated attacks of cellulitis and *lymphangitis* The distinguishing features of the varicose state, *i.e.*, petechiae, oedema and pigmentation, may be obscured by the superimposed eczema, but as a general rule the eczema and the capillary changes do not coincide in extent and the primary changes in the skin can be made out in some part of the leg.

Hypostatic eczema is notorious for its capa-ity to initiate general sensitization, the usual sequence being the appearance of an

eruption on the other leg, then the thigh upper limb peri-orbital area and lastly the trunk. Watson Smith [9] ascribes the general dissemination to unsuitable applications and inadequate bed rest Templeton postulates absorption of tissue products from the eczematous area and the appearance of circulating antibodies in the blood stream The question has been considered fully in Chapter IX Whatever the mechanism of dissemination may be, it is a very real danger which should be kept in mind when antipruritic or antiseptic applications are prescribed for an eczema of the legs

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Chapter XI

DIAGNOSIS

L. J. A. Loewenthal

THE subject may be conveniently considered in two sections: differentiation of the eczemas from other cutaneous disorders and aetiological diagnosis in a case considered to belong to the eczema group. It is in this chapter that lack of experience on the part of the reader and the limitations of written description and photographic reproduction will be felt most keenly: abler pens have failed to impart what should be an ocular demonstration. The difficulty is analogous to the task of learning to swim from text and illustration, but without immersing the body.

DIFFERENTIAL DIAGNOSIS

There is no difficulty in distinguishing the common appearances of an eczema from the common appearance of other dermatoses. The presence of erythema with several of the following—papules, vesicles, scales, crusts, weeping and lichenification—is usually enough to make a morphological diagnosis. This can be confirmed if necessary by the typical histological findings. But when either the eczema or the alternative dermatoses present in an atypical form certain difficulties may be encountered, the list of such conditions is short, for it is not my intention to devote space to conditions which are obviously non-eczematous; the reader must be credited with a certain amount of clinical acumen and with the knowledge that only itching eruptions are likely to cause difficulty.

Psoriasis of the scalp has already been referred to in Chapter VIII. When it affects the hands, feet and flexures this disease is frequently confounded with eczema. In the first place it often causes severe itching at these sites; secondly it rarely shows typical scaling and bleeding points and does not necessarily show the glistening surface seen on the toe in Figure 69; and thirdly when

affecting the palms and soles it frequently produces vesicles and pustules which may be mistaken for the pompholyx lesions of eczema

The first requisite in detecting such manifestations of psoriasis is to be aware of their possible existence; the second is to examine the whole body surface carefully in spite of the patient's insistence



FIG. 69
Psoriasis of the foot

that no other skin lesion is present. In many such cases psoriatic lesions of the scalp or finger nails will be found in others even the classical lesions on the elbows or loins may have escaped the patient's notice Without confirmation of this kind the differential diagnosis of flexural psoriasis and flexural seborrhoeic eczema is often difficult or for a time impossible Some help may be gained by observing the invariably sharp margin of psoriasis without undermining and without surrounding erythema but mistakes will occasionally be made by even the most expert The psoriasiform lesions occasionally seen as an exaggerated exampl of para keratotic or seborrhoeic eczema never show all the signs of psoriasis when scratched that is silvery scaling, a glistening base (*tache de bougie*) and pinpoint bleeding In order to accustom th- eye to the manifestations of psoriasis referred to above I recomm nd the

careful study of a series of cases. Too often, when the typical lesions on elbows, knees and trunk have been seen, such patients are studied no further yet it is in these that close and careful examination of the scalp, flexures, genitals and extremities will often reveal changes that can be memorized as typical of psoriasis in these areas. In this way a visual memory is established and



FIG. 70
Acute eruptive lichen planus in the fourth week.

when such lesions are seen subsequently without typical signs of psoriasis elsewhere, they are less likely to be called eczematous or seborrhoeic

Lichen Planus may be confused with eczema especially in an acute, eruptive phase; its differentiation from atopic *dermatitis* has been considered in Chapter IV Figure 70 shows such a case in the fourth week, the close aggregation of papules has produced the appearance of lichenification. In the early stages the absence of grouping of lesions in lichen planus may be significant, as may the complete absence of vesicles. Methodical examination of the patient, including the mouth will usually suggest the correct diagnosis, and this may be confirmed histologically

Non-eczematous Infective Dermatoses, such as impetigo, do not usually cause confusion; cases of acrodermatitis pustulosa however

are often mistaken for eczema. The important differential point is the presence of undermining in the infective conditions, so that a recognizable peripheral fringe is seen (Fig. 71). This is essentially identical with the fringed remains of the flaccid vesicle of acute impetigo.



FIG. 71
Chronic bacterial acrodermatitis, not eczematous. Note peripheral fringe.

Lichen Simplex Chronicus of Vidal (circumscribed chronic neuro-dermatitis, circumscribed pruritus with lichenification of Brocq). In this condition pictured in Figure 72, lichenification is produced by rubbing or scratching of one or more areas which at first itch *without visible signs. If it is remembered* that lichen simplex never *presents any of the other lesions described* as characteristic of eczema *there is little likelihood* of confusion with non-atopic eczema. Its differentiation from atopic dermatitis has been considered in Chapter IV.

Prickly Heat. Though rarely seen in temperate climates this *condition may be confused with eczema in tropical and subtropical* areas. *Unless eczema has been produced secondarily by infection* or over treatment prickly heat can be distinguished from widespread eczema by the complete absence of grouped lesions (Fig. 73).

Herpetic Lesions do not as a rule cause difficulty compared with eczema: their vesicles tend to be larger and more uniform in

size and age. Papular lesions are absent and, in zoster at least, the distribution usually provides the diagnosis. The occasional rare case of herpes simplex seen on the trunk or limbs can be puzzling; often its true nature becomes apparent only from its repeated appearances in precisely the same area

Pityriasis Rosea occasionally appears as a profuse, itching, papular rash and may be mistaken for endogenous eczema until the second or third week, when typical macular and plaque lesions develop by coalescence of individual papules.

Dermatitis Herpetiformis. When this disease is seen in its typical form, with bullae, urticaria and lesions resembling erythema multiforme, there is no chance of its being confused with the eczemas. As stated in Chapter IX, however it may for some time produce only papular or vesicular grouped lesions and in some cases a differential diagnosis may be impossible. This is especially the case when the rare, localized form is encountered (Fig. 74) Investigative aids are discussed later but they are never conclusive and the correct diagnosis may have to await the appearance of non-eczematous lesions.

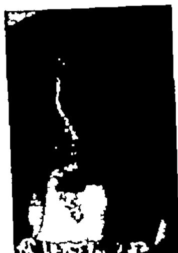


FIG. 7?
Lichen simplex chronicus of Vidal.

Ringworm should not, strictly speaking, be included in this section, for it can logically be regarded as a form of microbial eczema. Nevertheless, the circinate lesions of Microsporon infections of the glabrous skin and intertriginous lesions usually ascribed to *Epidermophyton spp* (but more commonly caused by Trichophyton) deserve special mention.

Tinea Corporis presents as one or more lesions of acute onset and rapid growth; a zone of activity at the edge shows vesicles or scaling and contrasts with the healing centre Such healing is the result of increasing immunity or diminished sensitivity to the fungus; when two or more growing rings meet the active edges of one lesion do not invade the central immune zones of others, hence bizarre lesions with polycyclic borders are produced. Tinea corporis tends to die out spontaneously when lesions persist, stop growing

are often mistaken for eczema. The important differential point is the presence of undermining in the infective conditions, so that a recognizable peripheral fringe is seen (Fig 71) This is essentially identical with the fringed remains of the flaccid vesicle of acute impetigo



FIG. 71
Chronic bacterial acrodermatitis, not eczematous. Note peripheral fringe.

Lichen Simplex Chronicus of Vidal (circumscribed chronic neuro-dermatitis; circumscribed pruritus with lichenification of Brocq) In this condition pictured in Figure 72, lichenification is produced by rubbing or scratching of one or more areas which at first itch without visible signs. If it is remembered that lichen simplex never presents any of the other lesions described as characteristic of eczema there is little likelihood of confusion with non-atopic eczema. Its differentiation from atopic dermatitis has been considered in Chapter IV

Prickly Heat. Though rarely seen in temperate climates this condition may be confused with eczema in tropical and subtropical areas. Unless eczema has been produced secondarily by infection or over treatment, prickly heat can be distinguished from widespread eczema by the complete absence of grouped lesions (Fig 73)

Herpetic Lesions do not, as a rule cause difficulty compared with eczema their vesicles tend to be larger and more uniform in

and no longer show the contrast of an active edge and quiescent centre, it is due to death of the fungus with the onset of bacterial infection. This development is usually accompanied by a marked diminution in itching, unless lichenification has occurred.

The appearances of tinea cruris and tinea pedis are too well known to warrant a full description. The latter diagnosis is made frequently but often wrongly (see remarks under "Topographical Diagnosis" later). In the great majority of fungous infections the lesions appear first either between or under the lateral three toes or in that part of the sole which, when wet, leaves no print on the bathroom floor. When the big toes and dorsa of the feet are predominantly affected a fungous causation is less likely.

The direct microscopic demonstration of fungal elements in scrapings from the active edges of the lesions, or in blister tops, is a simple and rapid procedure. It should be within the capabilities of every practitioner. Typical branching mycelium may, however, be difficult or impossible to demonstrate when fungicides have been used or when bacterial infection has supervened.

Intra-epidermal Carcinoma. Many varieties have been described and the lesions may resemble those of psoriasis or eczema. Paget's disease of the nipple is an example of an eczematoid carcinoma, usually associated with adenocarcinoma of the same breast. When well established it is indurated and there may be retraction of the nipple.

The condition may be confused with banal bacterial eczema of the nipples, frequently seen in nursing mothers, but also in nulliparae. In Paget's disease the edge is always sharply defined, there may be induration and a palpable subjacent tumour, and the condition is limited to one breast. Histological examination of a portion of the eczematoid skin is diagnostic. It should be undertaken early in all doubtful cases.

AETIOLOGICAL DIAGNOSIS

We now arrive at the goal to which the previous chapters have been leading. It has been shown how exogenous and endogenous allergens, microbes, alterations in acid-base equilibrium and constitutional factors can all be responsible for an eczema; it now remains to assess their relative importance in a given case. At the outset the reader is reminded that a clear answer is not to be expected every time; the fact that competent dermatologists dealing



FIG. 73
Prickly heat. Note absence of grouping of lesions.



FIG. 74
Localized dermatitis herpetiformis.

and no longer show the contrast of an active edge and quiescent centre, it is due to death of the fungus with the onset of bacterial infection. This development is usually accompanied by a marked diminution in itching, unless lichenification has occurred.

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with similar series will in the one case, attribute the majority to food allergy and in the other to psychosomatic effects should persuade us of this. The truth is, of course, that both authorities may be partly right: that in many cases of eczema there is a multiplicity of causes and that it is unwise to focus the attention too sharply on only one. True, sensational benefit usually follows the recognition and elimination of the chief cause in contact eczema, but occasionally disappointment and a healthy lesion in humility are encountered. We may make every use of skilful history taking and physical examination to cast strong suspicion on one or more external contactants; we may apply our patch tests *secundum artem* and find our suspicions confirmed. And having assured the patient that avoidance of the allergen in question will result in rapid recovery we find that after two or more weeks he is either no better or positively worse.

The understanding of such a *residual eczema* demands even more knowledge and judgment than does the original condition. It is in this class of case that familiarity with all the preceding chapters is essential. Was the condition in fact contact eczema or were the history and investigations misleading? Is this an example of latent atopy brought to light by a casual episode of contact eczema? Has the contact eczema actually cleared and been replaced by psoriatic lesions in the form of a Koebner reaction? Is a bacterial infection, an acquired or inborn inability to maintain the normal *p*H of the skin, or a second and third allergy to other contactants or to foods responsible, or can the persistence and aggravation of the eczema be attributed to autosensitization or psychogenic effects? Note again that in such cases neither the history nor the morphe alone can provide the answer: a consideration of both, possibly supported by investigative procedures, will be required.

In considering the diagnosis of a fresh case it will be found convenient to begin with a classification into atopic or non-atopic eczema. The personal and family history and the appearance of the eruption will often suffice to make a presumptive diagnosis of atopic dermatitis. It was emphasized in Chapter I that the morphe alone cannot be taken as a sufficient diagnostic criterion, nevertheless it is often sufficiently typical for the observer to decide that it is consistent or inconsistent with atopic dermatitis. The converse, however, is not true; it is never possible by inspection alone, to decide that an eruption is inconsistent with non-atopic eczema. Similarly, in differentiating the non-atopic eczemas, morphe and

distribution alone are not sufficient: an acute seborrhoeic dermatitis of the scalp and adjacent glabrous areas cannot be distinguished by inspection alone from an acute contact eczema caused by hair-dye.

To repeat the details of diagnosis of the various forms of eczema, already dealt with in previous chapters, would be superfluous. Some general remarks, however are called for. These will be unsystematic but they are planned to emphasize the difficulties which are so often encountered rather than to present an apparently easy road to success.

History

This is by far the most important single diagnostic measure available. Unfortunately it calls not only for a high degree of skill on the part of the dermatologist, but a reliable memory reasonable intelligence and strict truthfulness on the part of the patient; these qualities are not invariably present. The true art of history taking lies in obtaining an accurate chronological account of the development of the disease, and subsequently trying to identify factors which may be incriminated as causal. Remarkably few patients are able to give such a straightforward account of their complaint; time and again the unfolding of the story is interrupted by side issues which are quite irrelevant. The patient, however has made up his mind that these are the really important facts and great tact and firmness are often necessary to keep him to the point, that is to the chronological account of his complaint. A few examples are appropriate:

Q. So you were free of the rash during the whole of February?"

A. Yes, but that was when I wasn't eating tomatoes. You see I have noticed that tomatoes and all acid fruits.

Comment. It subsequently transpires that the rash has also been present when no tomatoes were eaten, and absent when they were. The diagnosis turns out to be contact eczema from certain plants, with periods of freedom when these plants were out of season. Nevertheless, though complete recovery has followed avoidance of these plants and though the patch test results have been demonstrated to her this lady continues to avoid eating tomatoes and acid fruits.

Q. What are your hobbies?"

A. I don't see what that has to do with my dermatitis. I have only had it since I started on this job and lots of my mates get this trouble.

Comment. Gordon's remarks on history taking in industrial cases may be quoted. "The merest hint that some preliminary investigation

may be necessary before the diagnosis is accepted brings the dermatologist's competence into question and induces a state of passive resistance The workman has never had anything wrong with his skin before he adopted his present employment his whole family for generations have been free from dermatological taint gardening cannot possibly have anything to do with it, because he only does a little of it over the week-end there is nothing wrong with his general health his blood is pure because when he cuts himself it heals beautifully half the workmen in his factory suffer from this complaint. To the lay public only two skin diseases are known The unemployed suffer from eczema and those in trades suffer from dermatitis"

The examples given above are illustrations of *prejudice* The patient has made up his mind and facts which run counter to his conviction are often suppressed as obviously irrelevant. The commonest fallacy in this connection is the belief that a substance must cause trouble at the first application how often do we hear that the nail lacquer cannot possibly be the cause of the trouble "because I have used it for fifteen years"? And how difficult it is to persuade the patient that it is she and not the nail lacquer who has undergone some change

But prejudice is not confined to the patient The enthusiast tends to find what he expects; different observers studying comparable groups, will find a preponderance of contact, bacterial dietary or psychosomatic causes according to which facet of the problem reflects the light of their scrutiny We have already seen that in many cases a multiplicity of factors is involved, and their elucidation may call for more than the average amount of time devoted to history taking. Hence *haste* is to be deplored as much as prejudice. Yet it is not always possible to devote to one patient the time necessary for a complete history taking and in such cases further questioning must be left to subsequent interviews—and even then some highly relevant fact may be missed

Thus a patient presented himself with an eczematous outbreak which had begun on the forehead and around the eyes and ears. General dissemination had followed within forty-eight hours. Now it is unusual for a seborrhoeic infective dermatitis to produce an autosensitization or bacterid eruption so promptly and the question of a contact eczema with dissemination in such a short time was equally unlikely Previous skin trouble was denied At the third interview the patient drew a wrist watch from his fob pocket during the course of conversation on being asked why he did not wear it in the usual place he replied that a rash had developed under the chrome plated watch strap two years previously Though this seemed irrelevant to the patient it made the diagnosis

obvious, the present attack had begun as contact eczema from a chrome tanned hatband and chrome plated spectacle frames the previous attack, caused by the watch strap, had sufficed to sensitize the whole skin surface and thus condition it for a universal outbreak as soon as the local contact eczema appeared about the head.

Thus the most important fact in the past history came to light by accident; more time spent at the first interview would possibly have revealed it.

The Snap Diagnosis often illustrates the errors into which haste can lead one. A patient presents a lichenified, eczematous rash involving the face, neck, hands, wrists and ante-cubital regions, and volunteers the information that he has suffered from asthma "for some time." It is tempting to waste no more time and to regard both manifestations as evidence of an atopic state, but it is wise to remember that both conditions can occur in the non-atopic individual from exposure to paraphenylenediamine or chloroplatinic acid.

The case history must thus include an enquiry into previous skin troubles, as well as the chronology and sequence of the present attack, with special reference to the presence or absence of a primary cutaneous focus. It must then obtain particulars often in the greatest detail, of occupation hobbies, seasonal and geographical factors and numerous other data which may show some relation to the course of the disease. The commonest of these, in my experience, is the indiscriminate use of topical, often proprietary remedies. Nevertheless, the patient is apt to scorn the suggestion that a widely advertised remedy (often cloaking its sinister properties under the title of "soothing salve" or "balm") can be responsible for much of his trouble; he is far readier to blame a reputable, almost certainly harmless preparation prescribed by a properly qualified medical man

Next, enquiry must be directed to the general health, especially to those systems which may provide a focus of bacterial infection: the presence of devitalized teeth, repeated attacks of tonsillitis, suspected gall bladder infection, pyelitis or prostatitis may all be relevant. And, finally the possible rôle of drugs must not be overlooked; the word "drugs" is better avoided in making enquiries, for most patients do not include in this category their laxatives, headache powders, cough mixtures, blood purifiers and haemorrhoidal suppositories.

Examination

It was stated in Chapter I that the morphe and distribution of an eczema cannot by themselves provide an aetiological diagnosis. They can however be highly suggestive, as in seborrhoeic and adult atopic dermatitis. In the former case the lesions will all approximate to the erythematous, scaly type, with or without



Fig. 75
Eczema of the eyelids, a common physical sign.

exudation in the latter to the papular lichenified pattern It is emphasized however that enough exceptions occur to preclude the use of naked-eye appearances as a *final* diagnostic feature. Two pitfalls (paraphenylenediamine eczema with asthma hair dye eczema) have been mentioned a third example provides perhaps the best illustration itchy red swollen scaly eyelids (Fig. 75) These are frequently seen as the only manifestation of contact eczema to substances conveyed by the fingers or directly applied (nail lacquer plant juices eyelash curlers) they may present as the major lesion in infective dermatitis, they are a common manifestation of atopic dermatitis they may give the first warning of dissemination from a primary eczematous focus; and they are frequently seen as an early feature of endogenous ecz ma

The history and physical findings, taken together are not necessarily diagnostic but they are an essential prelude to the use of investigative procedures. Widely distributed eczemas can in this

may often be provisionally classed as atopic endogenous or disseminated from a primary focus and, in addition, the stimulus for dissemination can often be surmised. The history can inform us of the primary focus and its change of character while examination enables us to distinguish the frankly infected areas from the secondary more truly eczematous eruption. The ability thus to distinguish the phases of an outbreak is essential for treatment and for assessing progress.

Investigative Procedures

It must be appreciated that these do not constitute a short cut to diagnosis. In dermatology as in any other branch of Medicine, specialized and laboratory tests may be invaluable in confirming or refuting a diagnosis; but they cannot be expected to take the place of meticulous history taking and physical examination.

Differential Diagnostic Skin Tests. It often happens that the history and clinical findings are not sufficient to distinguish an atopic from an eczematous dermatitis. In such cases useful information may be gained from the routine use of standard series of scratch tests with common atopens and of patch tests with common eczematogenic allergens (see Chapter IV Tables II and III) *Note that in this procedure we are seeking only to classify the case there is no attempt at defining the causal atopens or allergens*

Specific Diagnostic Skin Tests, intended to incriminate the actual causal allergen, are limited to the patch test (Chapter III) scratch or intradermal tests used for this purpose are not a recognized dermatological procedure

A patch test with 50 per cent. potassium iodide in soft paraffin is sometimes used to confirm the diagnosis of dermatitis herpetiformis. In practice it is of little value, for many cases of eczematous dermatitis show a positive reaction and a few cases of dermatitis herpetiformis pass through phases when the test gives negative results

Histological Examination. This is of importance mainly in the differentiation of the eczemas from other dermatoses The points of resemblance and difference between atopic and eczematous dermatitis have been demonstrated in Chapter V

Bacteriology The isolation of bacteria from an eczematous lesion is insufficient proof of their causative rôle. More significance can be attached to an eczematous patch test reaction, using filtrates of the suspected strains, but this method has not yet gained the wide acceptance it seems to deserve (see Chapter VII)

The part played by fungi may also be debatable. There is no doubt that the recognition of fungal elements, by direct microscopical examination is presumptive evidence of their pathogenicity On the other hand a positive culture, with a negative direct examination is not necessarily significant interdigital scrapings from apparently normal feet for instance, frequently produce a growth of dermatophyte and one may assume that this could obtain in feet affected by a *non-mycotic eczema*

The investigation of focal sepsis may be of great importance in diagnosis but does not properly fall within the scope of this work

Blood Studies. Eosinophilia often fluctuating in degree from day to day is a constant feature in atopic dermatitis and usually absent in contact nummular and seborrhoeic eczemas. In disseminated and endogenous eczema a moderate eosinophilia is sometimes seen counts of more than 400 per cu. mm suggest the possibility of dermatitis herpetiformis. The presence of anaemia or findings suggesting disturbed liver function may be relevant as therapeutic indications (*see* Chapter IX)

Elimination Diets. These are required to confirm the diagnosis of eczematous dermatitis due to food allergy and may also be useful in the management of atopic dermatitis. Such elimination diets[1] are, on the whole unsuitable as a diagnostic measure unless the patient is kept in hospital A few patients, however are able to lead an otherwise normal existence while being tested with Rowe's diet No 4 in this milk is the only food taken for two or more days and other foods are added singly if relief has been obtained.

Reproduction of Suspected Causal Conditions. We have seen that the patch test is not an infallible guide in the elucidation of contact eczema for the allergen is applied at a different time and often in a different form to a different area of skin Hence tests made with cosmetics may be positive when applied in the " V " area of the neck and negative elsewhere. In view of this occasional fallibility of the patch test it is sometimes necessary to reproduce the actual conditions under which the contact reaction is thought to have occurred. Thus, in the case mentioned above the patient would be asked to apply the suspected cosmetics singly once the eruption had subsided

In drug eruptions the patch test performed with the actual allergen may be negative, whereas the ingestion of a minute quantity

of the drug will promptly reproduce the eczema. This procedure is not recommended except in those rare instances when the identification of the drug is imperative; it is, as a rule, far wiser to leave well alone when an eruption has disappeared on withholding a drug. Severe and even fatal consequences have been known to follow the ingestion or injection of a drug to which the patient has previously shown an allergic reaction. Rarely however a suspected drug may be strongly indicated, for instance when an epileptic has shown intolerance to all other efficient anti-convulsants, or when a severe infection demands the use of a specific antibiotic. In such cases a minute test dose must be given under supervision and all necessary antidotes, including cortisone and ACTH, must be at hand.

A similar test by reproduction may be demanded in atopic dermatitis, but here there is little risk of dangerous effects; the only exception is when an infant with atopic dermatitis reacts to the ingestion of certain foods by a sudden and often alarming swelling of the lips and tongue.

The principal differential diagnostic features of some of the eczemas are tabulated in Chapter IV (Table I). As an additional aid the main steps in diagnosis are given in Table IX. This diagnostic key is intended to be a reminder only and cannot replace a full understanding of the nature of the various eczemas.

TABLE IX

KEY TO AETIOLOGICAL DIAGNOSIS IN THE ECZEMAS

1 The HISTORY and APPEARANCES suggest
  - A Atopic Dermatitis.
  - B Contact Eczema (with or without dissemination)
  - C Seborrhoeic or Infective Eczema.
  - D Non-atopic Endogenous Eczema.

2 NON-SPECIFIC INVESTIGATIONS (to determine whether in Group A, B, C, or D)
  - A. (i) Standard series of scratch tests show high proportion of positives.
    - (ii) Eosinophilia shown by repeated examination.
  - B Standard series of patch tests show high proportion of positives.
  - C All above tests show results not in excess of normal.

3 SPECIFIC INVESTIGATIONS.
  - A. (i) Elimination Diets
    - (ii) Elimination of Inhalants.
    - (iii) Demonstration of Passive Transfer Antibodies.
    - (iv). Histological Examination of the Skin
  - B Patch tests with substances suggested by history and appearances

C (i). *Reactions to autogenous bacterial products.*
(ii). Examination for fungus in primary lesion.
(iii). Search for infective foci.
D (i) Patch tests with *suspected drugs.*
(ii). Elimination diets.
(iii) Search for infective foci.

4 CONFIRMATORY or SUPPLEMENTARY Procedures.
A. Re-exposure to dietary or inhalant allergens.
B Re-exposure to contactants under conditions of original exposure.
D Ingestion of a suspected food or drug (the latter rarely necessary and possibly dangerous).

Common Causes of Diagnostic Errors

Accepting the Patient's Theories too Readily An example was given earlier in this chapter and every dermatologist will remember *many* others. Errors are most likely to be made when the patient's theory is nearly but not quite, correct. In one such case the lady was *insistent that* exposure to cold produced a palmar rash this she had noticed when helping in a café and serving iced drinks. *In actual fact she had a contact eczema from chrome and it was* the handle of the refrigerator and not the iced bottles, which *caused her exacerbations*

A similar fallacy is well illustrated by the following case:—

A young woman complained of recurrent itching, redness and swelling of the eyelids. She confessed that she had always been emotionally *unstable and was quite positive that each attack of irritation developed* a day or two after the onset of an attack of depression. This was confirmed by several reliable witnesses. It is not surprising that this history was taken as *prima facie* evidence of a psychogenic dermatosis and that she was referred to a psychiatrist with the diagnosis of "neurodermatitis." No blame can be attached to him for accepting the diagnosis, in view of the reported facts. Involvement of the eyelids was taken to mean an unconscious production of the appearances following "a good cry" After many months of treatment the attacks were still appearing a *more careful history was taken, this time* by a dermatologist, and it was discovered that the patient invariably countered an impending depression by a visit to her beauty specialist, to restore her "morale," as she put it. At these visits, and at no other time, nail lacquer was applied and other cosmetic procedures carried out. The patch test to nail lacquer was strongly positive and the skin trouble *has* not recurred since discontinuing its use.

Over Reliance on Skin Tests. It has already been stated *that* scratch and intradermal tests are of little specific use in management of atopic dermatitis *Even the patch test is significant* in contact eczema only when it confirms the tentative theory evolved

from the history and examination. As Sulzberger and Baer* have remarked: "Positive reactions to skin tests indicate simply that the individual has at some time previously been exposed to the agent



FIG 76

Contact eczema from nylon stockings. Such cases are frequently labelled epidermophytoses without adequate investigation.

(or to one of its immunologic relatives) and that his skin has become sensitized to it. The positive result does not necessarily mean that the agent is responsible for the lesion or symptom that brings the patient to you.

Haphazard Skin Testing is thus to be avoided. This must not be taken to refer to the use of routine series of tests in the differential diagnosis of eczematous and atopic dermatitis. But the infliction of a battery of tests, in the hope that a causal agent may thereby be revealed, is unscientific and deplorable.

Topographical Diagnosis. Though the error is puerile, experience shows that it is often perpetrated it is the commonest manifestation of the snap diagnosis. The reader is therefore reminded that not all eczemas of the scalp are seborrhoeic; some, indeed turn out to be psoriasis when the patient is properly



FIG. 77
Elbow flexure from a case of disseminated eczema of three months duration. Primary focus was a contact eczema from acriflavine Note resemblance to atopic dermatitis.

examined Not all eczematous lesions of the feet are due to fungi in my own experience considerably more than half are caused by bacterial infection or contact allergy (*see* Fig 76) Not all antecubital and popliteal eruptions are atopic dermatitis, yet they are frequently labelled "neurodermatitis" after a perfunctory glance

and sentenced to a course of psychiatry when they may be suffering from an infective flexural eczema or dissemination from a primary eczematous focus (Fig. 77)

The Term "Neurodermatitis," used to designate atopic dermatitis, is an unfortunate misnomer It is believed that atopic subjects may show emotional instability as one of the manifestations of their malady but this is no reason for incriminating the psyche or even the neurovascular system for all their troubles. The main reason for rejecting the word " neurodermatitis " is therefore the inevitable bias which it arouses in the user who is apt to concentrate on the patient s emotions to the exclusion of other more important factors.

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CHAPTER XII

TREATMENT—GENERAL PRINCIPLES

L. J A. LOEWENTHAL

DERMATOLOGY is often called an unscientific subject and unsystematic methods of treatment are adduced as evidence of this failing. The fact that the skin is so accessible to treatment has also determined that it is accessible to ill treatment; it is noteworthy that the hard words directed against the therapy of skin diseases often emanate from members of the "Try this" school We cannot improve on Goethe s "*Wir sind gewohnt dass die Menschen verhöhnen was sie nicht verstehen* (we are used to people deriding what they do not understand) The fact is that *the rational treatment of skin diseases and of the eczemas in* particular can show results superior to those obtained in most specialized branches of Medicine

It is significant that the best results are regularly obtained by the great masters This is not because they have at their disposal any remedies of greater efficacy than those available to others: rather is it the outcome of meticulous diagnosis of familiarity with the substances they use and the vehicle in which they are administered, and the attention they pay to the correct methods of application and removal This last essential provides one reason for the superior results obtained in specialized clinics. skilled nursing may *play a far bigger part in the management of the eczemas* than is generally realized In my own experience of a 600-bed skin department during World War II the average duration of stay in hospital fell by one third as the nursing staff gained experience, although no changes were made in the actual treatments prescribed.

To speak of a *cure* implies the recognition and elimination of an offending agent; even this does not invariably lead to prompt recovery unless we are able to overcome a secondary *train of events*, such as infection, lichenification or a morbid state of mind which may in *its turn* affect the diseased skin By curing we mean allowing the skin to recover this is possible only when the primary

causative agent is known and when all secondary noxae are dealt with simultaneously The simplest therapeutic successes are therefore seen in uncomplicated contact or microbial eczemas: here detection and avoidance of the allergen will, in the one instance, produce a cure, as will specific anti-microbial therapy in the other Yet we must not forget that some other less obvious factor may have been at work and that a person sensitized to one contact allergen may readily become sensitized to one or more others; a bacterial eczema, again, is often a sign that the skin's natural defences are faulty and that the "cure" of existing lesions is no guarantee against their recurrence.

When the nature of an eczema precludes a cure in this sense, as for example in many cases of atopic dermatitis and endogenous eczema, it is our duty to *alleviate* and above all to give *comfort* in every case. Often enough the dermatologist's reputation alone will give encouragement, but it is noteworthy that those with the greatest reputations place least reliance on this.

PREVENTION

Familiarity with the known causes of the eczemas enables us to lay down certain suggestions for prophylaxis.

In Industry prevention begins with the selection of personnel. Where there is a risk of contact eczema from some substance which is inseparable from the trade, the type of skin may be important. According to Schwartz, Tulipan and Peck, many factories will not employ persons with thin blond skin in these circumstances. The added hazard which is believed to accompany this type of skin may of course, be due to the relatively slight sebaceous secretion; this leads to a greater risk of chapping and secondary eczemas from soap and detergents, through the mechanism detailed in Chapter VI. Pre-employment selection based on the type of the young applicant's skin should rightly include an estimate of what the skin texture will be in twenty or thirty years time. The skilled workman whose skin has become vulnerable with the advent of middle age may represent not only a tragic figure but a greater economic loss to his trade than several unsuitable juveniles.

Pre-employment patch testing with the allergens likely to be encountered is not a helpful procedure as it cannot prophesy and at the worst may initiate a specific contact sensitivity The reliable history of a previous eczematous outbreak or the presence of eczematous or seborrhoeic lesions are a bar to employment where

the risk of contact sensitivity or exposure to non-allergenic irritants exists It is probable that pre-employment testing of the alkali neutralizing power of the skin would be of some use in trades which entail the frequent handling of lime (*see* Chapter VI)

Protection of the worker embraces such measures as dust extraction workshop cleanliness and the use of special clothing, masks and gloves Barrier creams do not replace other protective measures but may be a useful adjuvant in, or rather on, the right hands Personal cleanliness is desirable but too frequent and thorough use of soaps and even neutral detergents carries its own risks.

In Everyday Life over-cleanliness may also be a hazard the routine use of household antiseptics in washing is particularly to be deplored One of the most frequent causes of eczema and of the aggravation and dissemination of eczema is the haphazard use of potential sensitizing agents for minor skin complaints. It is surprising that mercurials sulphonamides, flavine, antibiotics and many other dangerous substances are still allowed to be sold so freely It is also regrettable that such substances are so readily prescribed by medical men without a clear idea of what they are intended to do and often with no conception of the harm they may cause Recognition and suppression of this abuse could be one of the most promising approaches to the problem of eczema In one of my series of 500 consecutive cases half of those suffering from contact eczema had been sensitized to topical applications[1] numerous authors, for instance Underwood *et al* have published similar findings

THERAPY—PRELIMINARY CONSIDERATIONS

Aetiological Management The importance of this has been stressed repeatedly further repetition should be unnecessary

Need for Caution. Though the rest of this work deals with the cure, alleviation and comforting of the eczema patient the principle of *primum non nocere* should always be in our minds. Being aware of the potential dangers of the methods we employ we should, in most cases, be able to avoid inflicting further damage or at least recognize and remedy such a mischance in its earliest stages.

The reminder that reasonable caution should be exercised must not, however be construed as advising too rigid adherence to old and sometimes unsatisfactory methods.

> " Be not the first by whom the new are tried
> Nor yet the last to lay the old aside "

Assessment of Success or Failure. The vast number of remedies advised for the systemic treatment of the eczemas argues the lack of standard controls This, as Twiston Davies remarks in another context, " shows clearly what can be done by a contented physician and a credulous patient between them. Sentiment, prejudice and suggestion take such a prominent part in treatment that control of a therapeutic assay has to be very strict and requires a much larger number of patients than are usually available." Many forms of treatment are published without specifying the types of eczema in which they have been used, hence the claim to *cure* a condition of such diverse aetiology is hard to credit, though it may be possible to *suppress* the signs and symptoms irrespective of the causation. To my knowledge there are no adequate figures available for the incidence of spontaneous recovery in the various forms of eczema nor for the degree and duration of the fluctuations that may be expected. Hence the appraisal of a suppressive remedy can be made only in the light of previous experience—usually an impression—or by the observation that repeated periods of administration in the same subjects produce invariable improvement, while withdrawal of the remedy is constantly followed by relapse. The undoubted beneficial effects of cortisone and ACTH are evaluated in this way

In the assessment of topical therapy *the method of paired comparisons* is logical and practicable. By treating symmetrically placed lesions with different remedies a rapid and unequivocal answer may be expected. The method deserves wider recognition.

SYSTEMIC THERAPY

Drugs

Of the multitude of remedies referred to previously only a *few* can be selected for consideration A full account would have to include every vitamin, every known hormone, every antibiotic and a generous selection of animal, vegetable and mineral extracts.

Cortisone and ACTH have gained universal acceptance for their ability to suppress the signs and symptoms of tissue reaction. It must, however be realized that they are suppressors and not curative agents and that permanent recovery follows their use only in self-limiting diseases or in cases where the skin can remain normal without further assistance, once complete healing has been achieved This is particularly seen in disseminated, presumably autosensitization, eczemas.

Although these hormones may be used for prolonged periods in controlling otherwise intractable cases they are also of great service in procuring temporary relief for instance during a journey or to prevent a severe flare-up when known adverse conditions are to be encountered They may be used in contact eczema in order to procure rapid relief even while patch testing is in progress, for their exhibition does not interfere with the development of specific reactions. In several cases observed by me the use of cortisone or ACTH has abolished a residual eczema by interrupting a vicious circle mechanism In these patients the identification and avoidance of the causative contact allergens had been without effect on the disseminated eczema other forms of systemic and local treatment gave at the best slight relief It is noteworthy therefore, that not only did cortisone produce complete relief from signs and symptoms, but that a relapse did not occur after its withdrawal Though symptomatic relief does not invariably result from the use of these hormones, it does so sufficiently often for us to state that ACTH and cortisone are far superior to all other remedies in the symptomatic management of the eczemas.

Dosage varies with the patient and should be based on that advised in the management of atopic dermatitis (Chapter XIII) To procure the quickest improvement an intravenous infusion of 20 units of ACTH administered over a ten-hour period is the method of choice maintenance therapy can then be given with oral cortisone The contra-indications usually listed seldom apply to a seven-day course of these remedies; more prolonged treatment calls for the precautions laid down in Chapter XIII At present the cost of these endocrine preparations is high and their use in consequence limited as it is often possible to procure improvement with cheaper remedies, details of some of these are given below

Arsenic is an old and valuable remedy which has fallen into undeserved disfavour for it is almost without risk when properly used. It is of most service in papular and lichenoid chronic eczema and sometimes in atopic dermatitis, and should not be given to the acute case or during a flare-up I give 3 to 4 minims of Fowler's solution thrice daily for a month and allow two months to elapse before repeating There is no danger of late sequelae from not more than three such courses Carbarsone (Lilly) is sometimes more rapidly efficacious and is given in shorter courses of one tablet of 0·25 gram thrice daily for two weeks

Sulphapyridine is a useful suppressor given in small doses and if necessary over many months. Using not more than four tablets of 0·5 gram daily I have treated over a thousand cases without untoward results and with good suppressive effect in more than half: these have included many cases of atopic dermatitis. Improvement is usually apparent by the end of the second week, thereafter the dose is reduced and maintenance by as little as one tablet daily can often be reached. Its mode of action is unknown, but in this dosage it is certainly not antibacterial. Previous intolerance to sulphonamides, or the suspicion that a sulphonamide application may have provoked an eczematous reaction are of course absolute contra-indications.

Sodium Para-aminobenzoate, in doses of two or more grams four times daily occasionally has a dramatic, but sometimes temporary beneficial effect. Weiner* first reported success with this drug in the treatment of atopic dermatitis, and my own experience suggests that it may be of benefit in contact, disseminated and endogenous eczemas. It has, however the property of encouraging bacterial growth and should therefore not be used in the presence of obvious sepsis.

Crude Liver Extract, by intramuscular injection, undoubtedly benefits many cases, especially of the seborrhoeic type seen in elderly people (see Chapter IX—"Nutritional Factors"). Unsaturated fatty acids, the so-called Vitamin F are widely used in certain countries but give disappointing results in others. A biotin deficiency has been postulated in certain forms of infantile eczema and deserves further trial in some non-atopic cases (see Chapter X).

Calcium and the so-called Anti-histaminics may exercise a moderate anti-pruritic effect in some patients. In the hands of dermatologists who collect their case records and assess results they have proved of little or no value in the routine management of the eczemas.

Sedatives and Hypnotics are indicated if they are likely to increase the duration of sleep or in other ways procure mental or physical rest for the patient. Apart from the suppressive remedies we have considered, there is no known drug which will relieve itching in the sense that opiates relieve pain. It is, in fact, wise to warn the patient that real symptomatic relief from a severely itching eczema will be obtained only when the eruption shows signs of subsiding. Some patients, however may experience partial relief from moderately severe itching if barbiturates are taken in my

experience these are quite useless in episodes of severe itching. In some persons the anti-histaminics exert a sedative effect but patients vary greatly in their response to particular compounds. Chloral is often helpful in adults, as in children bromides are uncertain in action and sometimes produce undesirable effects, for cases of endogenous eczema may show an intolerance to them as well as to iodides Opium and its derivatives are contra-indicated, they are not hypnotics, they do not relieve itching and occasionally indeed they aggravate it.

Rest

Relaxation is an integral part of the management of severe eczema The patient requires relief from the irritation of his daily round, from the effects of sweating produced by his normal activities and from the warmth of his clothes His skin benefits from an even temperature, the absence of friction and, above all from preventing the consequences of rubbing and scratching The control of itching is therefore one of our most important tasks. In this respect an unimaginative order to "stay at home and rest" may be the worst advice, but mental distraction even to the extent of occupational therapy can be of great value.

Diet

In atopic dermatitis and in those infrequent cases of non-atopic eczema due to food specific methods of elimination are indicated Many authorities have in addition urged a dietary régime in other varieties of eczema for instance in the seborrhoeic type (Chapter XIII) Strict dieting as a symptomatic measure, even in contact eczema has been advised by many writers and a full account of various methods is given by Urbach Some depend on absolute or relative starvation to correct a supposed alimentary dysfunction with others the aim has been to procure improvement by some specific change, such as an alteration of the chloride and water balances Urbach himself was impressed with the gratifying results claimed for so many different forms of diet and wrote. "When we consider the fact that in one instance total abstinence from food in another a diet of raw foods, and in still another an alkalinizing diet leads to marked improvement we must inevitably arrive at the conclusion that the common factor which promotes amelioration in acute epidermatitis lies in the rapid changes in the blood and tissue reactions brought about by any radical alteration in the diet" The fact which is not mentioned that many cases make excellent

recoveries without any dietary treatment whatsoever emphasizes earlier remarks on the assessment of success and failure.

Alcohol and highly spiced foods certainly produce flushing of the skin and sweating in many subjects. They are therefore likely to bring on an attack of itching and exudation in the eczema patient and should usually be forbidden. There are, however many people in whom moderate drinking has become a habit; in such cases complete withdrawal of the customary ration may cause more upset than the temporary vasodilatation which, in any case, is not always seen. I have yet to encounter a patient in whom the moderate use of alcohol has been responsible for preventing recovery: in cases where this has been suspected I have usually been able to find some other far more pertinent error in my management of the case.

Psychotherapy

Personal experience of a severely itching dermatosis would make better dermatologists of most of us. To add to the physical suffering which the patient has to endure there is a degree of mental stress which is sometimes insufficiently realized. In the minds of many is the belief that skin diseases are infectious, or at least the result of contamination with dirt; confusion with venereal diseases is still evident in frequent requests for a blood examination. Many believe that eczema is incurable and that they will have to continue suffering for the rest of their days. In most communities patients with skin diseases are shunned, more or less openly and even medical men and nurses do not always refrain from an expression of disgust when they inspect the diseased areas. Every woman, no matter how ill-favoured, fears disfigurement, and in both sexes lesions on exposed parts cause acute self-consciousness. These mental reactions are added to the trials of itching and sleeplessness and frequently produce a state of panic which is not appreciated by the medical attendant. If this panic is not allayed at an early stage there is a risk of the psychic trauma in its turn producing further deterioration in the skin, through the mechanisms outlined in Chapter IX.

The present-day tendency for patients to lie down on a couch and pour out their hearts to a psychiatrist, without having had the skin examined by a competent dermatologist, constitutes one of the greatest abuses of modern medicine and brings both specialities into disrepute. The services of a psychiatrist are, in any case, not particularly helpful in the majority for the patient needs to be

reassured by his own medical adviser The various factors referred to above should therefore be dealt with at the first visit and combated repeatedly on subsequent occasions It should not be necessary for the patient to ask whether the disease is infectious or whether permanent disfigurement will result an unsolicited reply to the questions which are troubling him carries far more conviction Reassurance may with advantage be taken to the point of *suggestion indeed, suggestion under hypnosis has been shown to* produce beneficial results in certain cases. [1]

The *prohibition of scratching is an almost automatic* piece of advice which bears examination Admittedly scratching damages the skin *produces flushing and sometimes further itching and* lichenification, and may add bacterial eczema to an uncomplicated case But does a simple prohibition have any effect? My belief is that far from checking the habit, it tends to add a burden of guilt to the patient s already heavy load of trouble and in many cases keeps his attention directed to his ailment more persistently than is desirable The doctor s advice is constantly repeated by the patient s relatives, who feel that they are thus doing something to help and ends by producing a state of exasperation which itself leads to further itching. The wise counsellor will tell the patient frankly that everyone with an eczematous rash scratches, and that they recover nevertheless, provided that the treatment is carried out in other respects. At the same time it can be pointed out that excessive scratching may delay recovery and that an occasional rub with a piece of clean gauze is preferable and just as effective. *Similarly when the patient states that those obvious excoriations* were inflicted in his sleep it is wise and humane to accept this *possibly untrue statement.*

TOPICAL THERAPY

The consideration of this important branch of treatment must not take precedence over aetiological diagnosis and systemic management. Nevertheless, though we regard it as ancillary and palliative, the symptomatic control of an eczematous eruption is the first consideration from the patient s point of view and the criterion by which he judges the dermatologist s competence. Without intelligent local treatment all other measures may be of little use; with it many sources of irritation may be eliminated, secondary changes prevented or counteracted *and the skin brought* to a state in which healing can take place

Some General Principles

At the risk of their being considered too obvious for mention, a few elementary principles of topical therapy and some prevalent fallacies are detailed. For a fuller treatment of some of these the reader is advised to read Sulzberger and Baer's discussion of common errors in the management of skin diseases.

Overtreatment. Our aim is to achieve the maximum result with the minimum of local treatment. More harm is done by the energetic use of powerful remedies than by the use of relatively inert ones. When faced with difficulties the question of what to leave off is of more importance than the choice of what to put on.

Method of Use. It is not enough to prescribe treatment: the patient and his attendants must understand clearly how remedies are to be applied and how they are to be removed, if this is necessary. Typed or written instructions should be given if there is any uncertainty.

The Vehicle is often more important than the ingredients. One often hears it stated that the local treatment of eczema is simple—if it is wet it must be dried with a shake lotion (calamine is usually mentioned); if it is dry it must be softened with an ointment. No axiom could be more pernicious. The former *treatment produces a hard*, uncomfortable and impermeable crust under which infection flourishes; the frequent unfortunate results of using an ointment just because the skin looks dry are aptly stressed by Sulzberger and Baer. An excellent rule regarding the choice of a vehicle is that *ointments should be the last to be considered*, not the first. They are occlusive and heating, and remedies incorporated in them exert a more powerful and less predictable action than when applied in tinctures, shake lotions or even pastes. In my opinion the last three vehicles are suitable for the majority of eczemas, from the subacute stage onwards, and instances of dissemination from a primary eczematous focus are rare when they are used, such dissemination is nearly always encountered when ointments are being applied. Further peripheral and adjacent spread of infective lesions are commonly seen with creams and ointments, even when these contain an antibiotic, and rarely under other vehicles. It is the lay mind which feels that an irritating eruption needs an oily or greasy application; medical practitioners unfortunately sometimes encourage this error and dermatologists should do more to educate them in this respect.

The last point concerns the method of applying ointments. as a rule they are smeared on thickly and quickly in spite of the direction "Rub in well and allowed to *spread over unaffected* areas, clothing and bedding. Used in this way they do the maximum *of harm with the minimum* of good For some years I have instructed every patient who needs an ointment not only to rub it in well but to wipe it off immediately afterwards with a face tissue or soft cloth This subterfuge ensures *that the patient will use less* ointment and will spend time on the necessary massage, for even *the wealthy feel* the waste of taking off as much as they put on and avoids the unpleasant results of excessive grease The beneficial effects of the application are certainly not prejudiced by this method.

Sting, Stink and Stain *Sulzberger and Baer*[1] *justifiably* condemn the haphazard use of disagreeable and painful topical remedies In children especially the use of tinctures in an alcoholic or other painful medium is to be avoided the use of unnecessarily rough cleaning methods is likewise to be deplored Dyes such as *gentian violet, fuchsin and brilliant green have their uses but these* must be weighed against the embarrassment they cause when applied to exposed parts and the staining of underclothes and bedding

CLEANSING

Too much disturbance of the diseased skin and the use of irritant cleansers undoubtedly retards recovery too little, on the other hand encourages infection by allowing exudate to be contained under crusts and prevents access of topical remedies to the skin when there is a collection of surface débris. Without going into details it *is as well to state that the necessity to remove the* last application is often an indication of an incorrect last application Shake lotions clogging on the surface and requiring frequent removal may suggest that compresses or tinctures would have been more suitable; an accumulation of grease is evidence of its *application in an improper manner if a paste has been* correctly chosen as the vehicle it is unnecessary to remove all of it at each dressing, for the addition of a fresh coating over the remains of the old does no harm I realize that these views may seem unorthodox to many but in my experience no harm has followed th ir adoption. Whether or not the reader agrees with this concept, he will agree that proper cleansing of eczematous areas calls for a high degree of nursing skill *when this is not available the reduction of* cleansing obtained by a more careful choice of vehicle may seem desirable

USE OF ACIDS AND MISUSE OF ALKALIES

The harmful effects of alkalies have been discussed in Chapter VI. They are frequently and regrettably used in the management of eczemas, either internally as citrate-bicarbonate mixtures, or externally as bicarbonate baths and compresses. Commenting on this, Wise and Sulzberger remarked, "The logical conclusion in managing many skin diseases is, therefore, not (as so popularly and inanely reiterated) to 'alkalinize' but rather to 'acidify'—at least as regards the skin surface."

An investigation by Schmid[7] into the reaction of ointment bases commonly used revealed that some were more alkaline than the normal reaction of the skin surface, and that the rest rapidly lost their slight relative acidity soon after application. He found that a buffered Lanette wax cream was satisfactory in procuring an initial lowering of the pH to 3·0 and a very gradual return to the normal range of 4·5 to 5·5. The result of clinical trials will be interesting.

Incorporating a mildly acid ingredient, for instance salicylic acid 1 per cent. or boric acid 3 per cent., is often a useful adjuvant and the popularity of these in many prescriptions may depend on their acidifying rather than on their keratoplastic and antiseptic properties. Personal experience makes me believe that either of them enhances the action of Vioform (Appendix B, Nos. 33 and 34). The preference shown by some clinicians for tars of vegetable origin (oleum cadini, rusci) may possibly be explained by their relative acidity when compared with mineral tars.

SOME TOPICAL REMEDIES

Little is known of the precise action of the many agents we use, and their further study by the method of paired comparison might even to-day produce some surprises. They may here be classified according to their supposed effects: details of their strength in various vehicles are given in Appendix B.

Anti-pruritics. Menthol, camphor, phenol, chloral hydrate, benzocaine and other local anaesthetics,* so-called anti-histaminics, possibly salicylic acid.

"Anti-eczematous" Agents are supposed to owe their effect to a "reducing" action as well as to their keratoplastic and keratolytic properties. The tars are probably the most widely used and may

* These agents have a relatively high sensitizing potential and are especially to be avoided in cases showing the effects of previous over-treatment.

owe some of their efficacy to a local desensitizing action It must be remembered that coal tar exerts a *photodynamic effect* and must not be applied to uncovered areas within twenty-four hours of exposure to *sunlight* Other commonly used remedies are ichthyol resorcin and salicylic acid. The choice of agent often varies with the whim of the dermatologist and the selection of topical remedies, but not of the vehicle remains an *empirical part of an unscientific* subject.

Anti-microbial Agents. The more useful antibiotics are listed in Appendix B (No 8) where, it will be noted, penicillin has been omitted Not only has it a relatively high sensitizing potential but recent bacteriological studies, *at least in South Africa show that* surface organisms are rapidly becoming *penicillin resistant.* Vioform *(Ciba) is* one of the most satisfactory agents available and can be incorporated in powders shake lotions starch poultices pastes, creams and ointments; cases of sensitization from its use are, in my experience, extremely rare. Mercury * in aqueous solution, cream paste or ointment is effective in some cases and combines *well with tar The danger of prescribing the ammoniate of mercury* with salicylic acid has again been stressed recently Silver nitrate, the dyes previously mentioned and tannic acid are also used as anti bacterial agents and may be preferred for children in whom relatively simple forms of application are often advisable; it is *possible that much of their value derives from their* astringent properties In treating eczematous lesions caused by the presence of dermatophytes first principles must not be *forgotten though the* unsaturated fatty acids are generally satisfactory their use in an ointment base during the vesicular or weeping phases is incorrect The same criticism must be levelled at the unimaginative, routine prescribing of Whitfield s ointment, without regard to the stage of *the eruption*

PHYSICAL METHODS

Rest is as important in topical as in general management In chronic lichenified lesions this may often be obtained by a firm, occlusive dressing for example with a zinc-gelatine bandage. The use of splints to prevent scratching is a measure which may have to be employed and, after the inevitable initial resistance, is often appreciated *by the patient. Splinting of infants* limbs, or tying their wrists and ankles to the sides of the cot is often advised a more acceptable method is to secure *the wrist bands of both sleeves to*

Ref footnote on page 13

the front of the diaper A better method consists of attaching tapes to the ends of the sleeves, crossing the infant's arms over its chest, and tying the tapes at the back. A strait jacket employing this principle is most suitable.

Alteration in Temperature. Vehicles for topical remedies, such as powders, compresses and shake lotions, owe some of their efficacy to their cooling action Alcohol and other volatile liquids act in the same way The alternate use of inert hot and cold applications, such as normal saline, is sometimes an effective anti-pruritic.

Trauma. As relatively harmless substitutes for the natural desire to scratch, light rubbing of an itching area or tapping with th fingers may be effective. Pinching of an adjacent area of normal skin is found to be satisfactory by some patients and it is not uncommon to see bruises produced outside an eczematous area.

Radiation is an important adjunct to treatment and X-ray therapy is of the greatest use in many forms of eczema. Though its mode of action is imperfectly understood it tends to reduce itching and inflammation when properly employed, and may have local desensitizing properties It is tempting to associate the last named effect with the well-known radiosensitivity of the lymphocytes and their suspected rôle in the allergy of eczema, but the experiments quoted by Haxthausen in Chapter III make this mechanism improbable. The following are generally accepted as standard principles:—

1 Acutely inflamed, weeping areas are unsuitable for X-ray therapy

2 As only a superficial effect is required voltages of 70 kv or less with unfiltered rays are advisable; in certain countries the administration of unfiltered rays is still construed as carelessness by courts of law and in these a "token" filter of 0·5 mm of aluminium should be used.

3 In all but the most torpid, chronic eczemas a maximum weekly dose of 75 r and total not exceeding 500 r should be employed. This fractional dosage may be divided into sub-fractional moieties of 38 r once or twice weekly if additional caution is indicated.

4 The area irradiated at one treatment should not exceed one quarter of the body surface.

5 It is possible that even cautious irradiation of an eczematous area may initiate a general dissemination. If premonitory symptoms

of itching at distant normal areas are experienced it is therefore advisable to interrupt X-ray therapy

Grenz (Bucky) rays, being of lower voltage and longer wave length have less penetrating power and are suitable for the treatment of eczemas. In general dosages are higher but the risks of permanent effects of overdosage, especially to deeper structures, is far less. But where the limitations set out above are observed there is no risk of damage from superficial therapy with X-ray machines customarily used by dermatologists.

The above guide is intended for those who wish to discuss dosage with a radiologist. The dermatologist who uses his own X-ray equipment will presumably have had suitable training. It is preferable for dermatologists to be equipped with the necessary apparatus and knowledge, so that the condition of the skin can be checked at the time of each treatment and the necessary adjustments made promptly

Thorium-X provides a method of administering non-penetrating alpha radiation I have used it with some success in a varnish or alcohol medium for treating areas of chronic, lichenified eczema. It is painted on in a concentration of 1 000 to 1,500 electrostatic units per ml at intervals of two to four weeks.*

Ultra violet light therapy is little used in the treatment of eczema in most cases it is of doubtful benefit and in many it can be positively harmful

Thorium X preparations have a very short effective life, but modern air transport enables them to arrive with the effective charge in distant parts of the globe.

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CHAPTER XIII

TREATMENT OF THE VARIOUS ECZEMAS IN DETAIL

1. MANAGEMENT OF ATOPIC DERMATITIS

VICTOR H. WITTEN and MARION B SULZBERGER

IT is logical to divide the discussion of management of atopic dermatitis into

1 General considerations.
2. Etiologic management.
3 Symptomatic management.

In that the infantile form of atopic dermatitis (infantile eczema) presents certain features and problems which differ from the childhood, adolescent and adult forms, its treatment is considered separately

MANAGEMENT OF THE INFANTILE FORM OF ATOPIC DERMATITIS (INFANTILE ECZEMA)

1 GENERAL CONSIDERATIONS

It is worthwhile to instruct the family (mother father grandparents, etc) in some simple facts as to the nature of the disease. Understanding of the following points will generally be reassuring to the family and lead to better co-operation and more intelligent management of the patient.

(a) As a rule, the baby's general health and well-being will not suffer regardless of the severity of the " eczema "

(b) Complete recovery can be expected in most cases about or before the age of two years.

(c) There is little danger of " infection " or " blood poisoning," despite all of the rubbing and scratching, providing the medications are used properly

(*d*) The condition is not infectious or contagious

(*e*) No physical marks or scars will result from the eruption

(*f*) There is no likelihood of psychic scarring. In spite of the apparent suffering (*which is not as bad as it appears to the family*) there will be no memory of the episodes when the baby recovers.

2. Etiologic Management

(*a*) ***Environmental Exposures***—*the atopic baby should be protected as much as possible from those exposures which are likely to prove detrimental these include, dusts feathers, wool silk animal sheddings certain cleansers, alkalis, acids, vapors and various micro-organisms rapid or excessive cooling and heating; high humidity and other environmental stresses.*

Towards this goal

(i) The room temperature should be kept even (about 68 F)

(ii) *The clothing should be soft light and cool cotton or linen* should be worn next to the skin in preference to wool or other rough materials

(iii) Soap should be avoided and clothes diapers, etc should be well rinsed after laundering.

(iv) *Possible food allergens should be eliminated* These are discovered by close observation of the effects of food elimination and re-exposure to suspected food. This method is more successful than the results of many hundreds of skin tests It is generally agreed that the common dietary allergens are (listed in their order of importance) cow s milk wheat and other cereals, eggs, citrus fruits, spinach peas tomatoes fish and fish products (including fish liver oils)

(v) *Make it routine to strip the infant s room* of excess drapes, rugs, stuffed furniture, blankets, etc Also in the attempt to reduce air-borne allergens, *the more allergenic types of mattresses* and pillows should be replaced with foam rubber or sterilized horsehair ones

(vi) *When other methods fail* remove the baby from its original environment. Change of environment often results in rapid and spectacular improvement *In a high percentage of infants mere* hospitalization will clear up the dermatitis often without any other therapy being necessary

(*b*) ***Specific Hyposensitization would appear to be Logical***—but unfortunately hyposensitization is of very little if any practical

value in the management of infantile atopic dermatitis. This is true even in the few cases in which a single specific allergen, such as wool or a food, is strongly suspected as being causative.

3 Symptomatic Management

The most promising symptomatic approach is that directed toward

(a) Removal of crusts and scales
(b) Combatting of infections.
(c) Soothing of irritation and alleviation of itching.
(d) Prevention of scratching and injury to the skin.

(a) Removal of Crusts and Scales.

1 Sponge or bathe in tepid tap water or water containing

(a) Bran starch, or oatmeal.

(b) Tar (liquor carbonis detergens or oil of cade) Soap should not be used.

Baths are given once to twice daily to once every few days. If not tolerated, they should of course be discontinued.

2. After *each* bath—or when necessary in lieu of the bath—the following procedures should be carried out:

(a) Careful removal of all scales, crusts and débris. Wet compresses or cleansing are often helpful (Prescriptions 1 2, 3 4) Soaking with, or application of, mineral or olive oil (or Prescription 5) will also facilitate separating adherent crusts, etc.

(b) Dusting liberally with a finely powdered talc or other mild dusting powder (Prescription 7)

3 In order to achieve the fullest therapeutic benefit, these modalities for removing crusts and scales should also be used prior to applying selected topical medications listed below

(b) Combatting of Infections.

While the ordinary amount of superficial infection superimposed on the eczematous areas usually responds very satisfactorily to the routine measures of bathing, cleansing, and the anti-eczematous topical agents (see below) it is sometimes necessary to use more specific measures. These consist of:

1 The topical application of one of the newer antibiotic ointments or creams, *e.g.* Bacitracin, Neomycin Gramicidin, Aureomycin, Terramycin or various combinations of these. It has been

See Appendix B

our experience that *these are often helpful anti-bacterial* preparations with a much lower index of sensitization than penicillin or sulfonamide ointments

2. Cleansing and/or compressing with solutions prepared with antibiotic solutions (Tyrothricin Neomycin Bacitracin etc)

3 Combining antibiotics with the older anti-eczematous remedies (Prescription 8)

4 *Oral administration of the antibiotics* Many of the antibiotics are now available in forms which permit the administration of small doses and which are usually palatable and easily given to the infant.

(c) Soothing of Irritation and Alleviation of Itching

There is no question but that the proper selection of topical medications for any particular case will prove to be the most helpful therapeutic approach for the baby with atopic dermatitis. Perhaps the future will see greater benefits through the systemic administration of cortisone or adrenotropic hormone (ACTH)

The scalp and face are the parts most often involved in infantile eczema *they are also parts most difficult to treat because of the* proximity to the ears nose and mouth and the problems of removing crusts and applying dressings etc

SCALP The crusts and scales should be removed according to the methods already outlined Usually twenty-four to forty-eight hours devoted *to cleaning up the area is required* before more active therapy can be started Prescriptions 9 10 may then be used These ointments should be removed gently with olive or mineral oil before reapplying under properly fitted dressings at least twice daily In that the scalp usually tolerates potential irritants better than other parts of the body it is often safe to use a bland soap (or a mild detergent) to wash the scalp several times a week.

FACE: The crusted and more severely involved areas may be cleansed without benefit of dressings which must remain in place around the clock Careful *gentle cleansing with cotton soaked in* oil (or in Prescription 5) or wet with one of the mildly antiseptic and astringent solutions (Prescriptions 1-4) should be done many times a day When wet compresses of Prescriptions 1-4 are used they must be applied correctly and carefully whether the open or closed method is used

Continuous care is essential and therefore Prescriptions 6 8 9 11 *should be rubbed in gently and reapplied as frequently* as is necessary to keep the areas covered

Usually within two to three days the worst of the crusting will be gone, and other medications may be applied. One of the best measures consists of the use of undiluted tar (Prescription 12) applied to the face under a mask. The crude coal tar is applied in a thick layer and its surface dusted liberally with plain unscented talc; over this a well-cut and pre-fitted mask is smoothly applied and carefully bandaged in place. This is removed after one to three days, when a face mask with plain or borated petrolatum is applied for twenty-four hours. These alternate applications of tar and plain petrolatum masks are repeated several times, if found helpful. (The body must not be exposed to sun when tars or other photosensitizing agents are being used.)

When improvement is noted, or a rest from face masks is desired, Prescriptions 11 13 may be rubbed in gently

TRUNK Because of the extensive areas involved and the difficulty and dangers of applying restricting bandaged dressings, the trunk does not generally lend itself so well to treatment with ointments.

Bathing or cleansing with the solutions previously mentioned are relatively simple measures and may be followed by the innunction of an ointment such as Prescriptions 6, 8 11 13 Large body areas are usually more easily managed by the application of "vanishing" type creams (Prescriptions 6 14) or of shake lotions or liniments (Prescriptions 15 16 17 18) or of medicated oils (Prescription 19) Of course large surfaces of the body should not be treated with preparations containing high concentrations of tar phenols, cresols, resorcin, etc., because of the danger of absorption and resultant systemic toxic effects. Lotions and liniments are best applied with an ordinary flat paint brush and the new application may be painted right over the old. When the caking becomes excessive, the area should be cleansed by bathing or gentle swabbing with one of the recommended oils or solutions.

At times, heavy pastes (Prescription 13) may be used and when dusted over with plain unscented talc usually adhere well and act as a protective covering for the involved part. Various medications may be incorporated in such a paste (e g Prescription 13) and because the active ingredients are usually not as "active" in pastes (lesser contact and delivery to the skin) they may be prescribed in greater concentrations.

Needless to say the greatest therapeutic successes will be achieved through the physician's familiarity with the properties of the preparations he prescribes, what can be expected of them; how

they should be applied and removed, together with conscientious and patient instruction to those who will care for the baby

All of the measures just discussed are intended to soothe and relieve pruritus In some instances however itch "crises" may be relieved by the application of hot (avoid burning) and at times cold (avoid freezing and chilling) compresses for a few minutes at a time.

Sedation (Prescriptions 21 22) sometimes proves helpful in intractable pruritus. The sedative effect of some of the so-called antihistaminics (Prescription 23) may be tried to produce mild sedation and to help promote sleep

(d) Prevention of Scratching and Injury to the Skin.

In addition to the above, in desperate situations physical restraint may be resorted to by tying the extremities to the bed, using splints on the arms or placing metal or plastic cups on the hands

MANAGEMENT OF ATOPIC DERMATITIS IN CHILDHOOD ADOLESCENCE AND ADULT LIFE

While many of the measures used in the treatment of infantile eczema are applicable in the management of atopic dermatitis in children adolescents and adults there are certain variations which are important

The selection of therapy will depend on the form of the dermatitis. In younger children where the eruption is more exudative, the treatment will be similar to that used in the infantile form The older the patient however the more the tendency to drier and thickened lichenified involvement which is best treated by the procedures to be outlined for the adult form of atopic dermatitis

1 General Considerations

As for the infantile form of the disease, it is advisable to give both the patient and the family some understanding concerning the nature of the process. While most of the points made for infantile eczema are applicable here, there are certain exceptions:

(a) The childhood phase of the eruption often disappears spontaneously but in some few instances continues or recurs within a few years as the adolescent form.

(b) When the disease is still present in the late twenties it is usually quite difficult to manage and the chances for spontaneous recovery are much reduced

(c) Only the suffering which occurs with the *most severe* forms of the disease is remembered by the patient. This memory does not interfere with eventual complete and satisfactory adjustment to a normal way of living.

(d) Today hope may be offered even to those who suffer the worst degree of involvement. The introduction of such new drugs as ACTH and cortisone, and more recently hydrocortisone acetate and free alcohol for topical use, present great promise for therapeutic effectiveness.

2. Etiologic Management

The discussion concerning environmental exposures as given for infantile eczema also holds for older individuals with atopic dermatitis. It is of value to dress properly avoiding heavy coarse and occlusive clothing (e.g. wool); to avoid excessive exposure to alkali soaps (many soap substitutes are now available); to make one's living quarters as "allergen free" as possible; to avoid sudden and extreme changes in temperature, etc.

The most exhaustive testing of the skin by the scratch or intradermal method or even demonstration of Prausnitz-Küstner antibodies in the blood serum are usually of little or no value in *finding* the specific offending allergens. When a particular contactant or food is *known* to produce flare-ups through clinical exposure it should, of course, be eliminated. For instructions on the "Preparation and Maintenance of a Dust Free Room" and suggested elimination diets, appropriate texts should be consulted—for example: Dermatology: Essentials of Diagnosis and Treatment."[1]

There is no question but that a change of environment, usually to a warm and dry climate, is beneficial even to the most chronic cases, even those failing to respond satisfactorily to all known methods of treatment (with the possible exception of ACTH or cortisone).

The present methods of specific desensitization are, unfortunately, of no real value in the treatment of atopic dermatitis.

3. Symptomatic Management

The therapeutic approach in the childhood, adolescent and adult forms of atopic dermatitis is dependent upon the presenting characteristics of the eruption. When in the eczematous phase, the treatment as previously outlined for the infantile form is applicable, where the goal is to remove the crusting, combat infection, soothe irritation, alleviate itching—in all, to dry the eruption and promote

healing. As the drying is achieved the selection of therapy changes and attention is directed toward removing scales, softening the hard skin reducing the thickening and infiltration and controlling the pruritus Alleviation of the severe itching that accompanies atopic dermatitis is perhaps the most important step in the treatment of the disease. This may be achieved by topical or systemic measures.

While there are admittedly many measures which are helpful in relieving itching Prescriptions 24 25 26 27 have been found to be particularly efficacious in many cases It is understood however that irritation is encountered in a certain percentage of cases Benzocaine (ethylaminobenzoate) should not be used unless existing allergic sensitivity has been ruled out and the patient is followed regularly Judicious use of the various tars in lotions, oils emulsions, ointments and creams is still one of the best therapeutic approaches as in infantile eczema

For many months we have had an opportunity to use hydrocortisone acetate in various concentrations in selected bases. A 1 per cent to 2½ per cent. preparation in a carbowax-type base has been efficacious in our hands More recently the hydrocortisone free alcohol has been used similarly in the same carbowax-type base with promising results *

When other methods have failed, several treatments with X-radiation will often prove helpful Grenz rays in our experience, are in many instances quite as effective as roentgen rays in the treatment of resistant patches of lichenified and pruritic atopic dermatitis. This latter modality permits a limited repeated use over the years, in contrast to the absolutely limited dosage permissible with roentgen rays

With the exception of cortisone or ACTH the effects of systemic symptomatic treatment are usually neither rapid nor striking.

When properly used there is no more effective therapy than systematically administered adrenocortical hormone or cortisone. It has been our experience that doses of 150-200 mg of cortisone orally given daily in divided doses produce a prompt and favourable response with 75-90 per cent improvement within a few days in most cases The dose is then reduced as rapidly as the patient's condition will permit. We have been able to retain patients on a minimum maintenance dose for many months without undue undesirable drug effect Such doses have varied from 100 mg. daily to 5 mg every second to third day Of course every necessary precaution must be taken with the patient using these drugs. These

include careful history taking for evidence of tuberculosis, gastric or duodenal ulcer diabetes, psychoses, etc., weekly recording of blood pressure and weight and routine urinalyses; and blood chemistries for sodium, potassium calcium and glucose levels at regular intervals and whenever indicated. (*See* Marion B Sulzberger Some Aspects of ACTH and Cortisone in *Dermatology* Tenth International Congress of Dermatology London, July 1952. also reference)

Other measures of management of atopic dermatitis in adolescents and adults include the following:

(*a*) Correct any discoverable abnormalities which may be interfering with general health and comfort.

(*b*) Endocrinologic approach All forms of gross endocrinologic dysfunction merit attention. Thyroid is occasionally of value when the skin is particularly dry and there are follicular hyperkeratoses.

(*c*) General dietary management. Other than the elimination of causal allergens a properly balanced diet should be maintained. Large doses of vitamin A are thought to be of value in some cases.

(*d*) Antibiotics. In selected cases where superficial infection is apparent, or a flare-up is known to be associated with or has followed some unrelated infectious process, *e.g* sinusitis, nasopharyngitis etc., the oral administration of penicillin 600,000-1 000,000 units a day or terramycin 1,000-2,000 mg. daily or aureomycin 1,000-2,000 mg daily in divided doses is often helpful. The dose is best gradually reduced rather than abruptly discontinued. Vitamin B complex in large doses is helpful in reducing the unpleasant gastrointestinal effects.

(*e*) Whenever possible, improve sweat gland function and water evaporation. Proper air conditioning is often a help in some cases. Certainly a high, dry and warm climate (such as Tucson, Arizona or El Paso Texas) is of value in the majority of cases.

(*f*) Whenever possible, reduce psychic and emotional tensions to their lowest possible levels. The benefits from this sort of protection may be related to the mechanisms operative under (*e*).

(*g*) Sedation or similar measures. In addition to chloral hydrate (3¾ to 7½ gr.) and phenobarbital (gr ¼ to 1) several times daily the antihistaminics " occasionally have a sedative effect when given in adequate doses.

A very small percentage of patients with atopic dermatitis develop cataracts or other ocular abnormalities. Therefore, all patients require periodic ophthalmologic examinations and, of

course, specialistic ophthalmologic management whenever the lens is involved

2. TREATMENT OF SEBORRHOEIC DERMATITIS

G A. GRANT PETERKIN

In most skin diseases one must remember that treatment of the individual patient, including all the multiple essences that contribute to the formation of his body and his mind, is quite as important as any local treatment which may be indicated. In seborrhoeic dermatitis this is particularly the case, as a full understanding of the patient may make all the difference between success and failure

LOCAL TREATMENT

The Scalp. A well known humourist has remarked that a French doctor invented the only cure for dandruff—Dr Guillotin. There is some truth in this assertion for it is usually easy enough to get rid of a pityriasis simplex capitis, but it is almost certain to relapse. Many treatments have been recommended for simple dandruff and most are reasonably effective so long as the patient fulfils his part of the contract For women and patients with oily scalps, lotions are usually prescribed, the amount of oil used depending on the individual requirements, *e g* Prescription 28

For men an ointment or cream can be given, or the medicaments can be incorporated in the hair-dressing they normally use or in a suitable base, *e g* Prescription 10

A popular new remedy from America is Selenium Sulphid Suspension (Abbott) but its value has not yet been completely assessed.

In the mind of the layman, shampoos are reckoned to be important for the health of the scalp but the person with an ordinary dandruff will find that toilet soap is probably as good as anything. In the presence of inflammation of the scalp it is wiser to use a non-irritating preparation such as 1 per cent cetrimide, *e.g* cetavlon (I C I) or one containing sulphonated lorol and lanette wax such as Ethisan (Crookes)

Should the scalp show excessive scaling redness or crusting different therapeutic measures are required Many of these patients will speedily respond to one of the quinoline derivatives such as Prescription 29 If the disease is chronic and severe more drastic

steps are necessary and the head may have to be shaved. The affected areas are painted with gentian violet (1 per cent. aqueous solution) night and morning, with a dressing consisting of a bland grease such as 1 per cent. ichthammol paste night and morning every third day. This treatment is used until there is no exudation, when crude coal tar is painted on like a thin varnish dusted freely with talcum powder to dry it completely and repeated every fourth day the bland paste being used as spreads on the previous one.

In *infants* slightly different treatment is indicated. Ordinary dandruff or "scurf cap" can be treated by an ointment such as ½ per cent. precipitated sulphur and 1 per cent. salicylic acid in unguentum emulsificans aquosum (B.P.) rubbed in gently twice a day but the presence of exudation renders a thick paste desirable, *e.g.* 1 per cent. ammoniated mercury in Lassar's paste, applied as a spread. Once the acute phase has subsided, a tar preparation such as ½ per cent. crude tar paste or Ether Soluble Tar Paste (Martindale) can be substituted. When circinate scaly red patches, not unlike ringworm, are in evidence these tar products or Vioform cream (Ciba) are usually successful.

The Beard Area. The term "seborrhoeic" has been applied to many beard lesions, from a few scattered follicular papules to a full-blown sycosis. The milder cases tend to clear up with simple treatment, *e.g.* 2 per cent. ichthammol in calamine lotion, but often stronger antiseptics must be used. Of these, the quinoline derivatives are the most valuable, prescribed as either Sterosan ointment (Geigy) or Ung. Quinolor Co. (Squibb) smeared on thinly and gently night and morning. It is important to warn the patient to stop them on any sign of undue reaction. The antibiotics have a limited field and are apt to provoke contact dermatitis, particularly penicillin cream and streptomycin ointment. The most effective is aureomycin ointment, but some find that terramycin and neomycin ointments are reliable. Neomycin-gramicidin ointment (Squibb) is one of the most recent but is not always effective and like the others can produce contact dermatitis. Occasionally a case which has proved resistant to other remedies responds admirably to an aniline dye such as 1 per cent. brilliant green and 1 per cent. gentian violet in 10 per cent. industrial spirit, but the individual naturally prefers not to use such colourful treatment. Of the many other remedies, one can mention 50 per cent. precipitated sulphur in petroleum jelly and alibour water either dabbed on or applied as a compress in a dilution of a teaspoonful to a pint of warm water

Superficial X-ray therapy is not infrequently advisable and should be used in fractional doses e g 75 r units once a week for four or five treatments On this location, shaving methods are important. Many find that an electric razor solves their difficulty but not too close shaving with a Gillette type of razor a bowl of soap and a clean brush are quite suitable.

Particularly if the upper lip is involved the nasal passages may have to be treated for instance, with vioform powder

Flexural Areas. Folds of the skin such as the ears, natal cleft and axillae, *require treatment similar to the scalp The most effective* application for moist lesions is Castellani s basic fuchsin paint diluted with equal parts of distilled water though silver nitrate (2 per cent. aqueous solution) may be used. After the paint, crude tar can be applied as on the head Quinoline drugs and antibiotics must be used with caution in the flexures, but thick pastes such as Lassar s or 1 per cent sulphur-salicylic paste are useful For these cases Kennedy (personal communication) recommends 4 per cent *sulphur in Lassar s paste. In the few patients who may be resistant,* fractional doses of X-rays are indicated.

Seborrhoea Corporis. The treatment of Seborrhoea Corporis is ordinarily simple and straightforward The vast proportion get better in two or three weeks with the use of 1 per cent. sulphur *salicylic ointment night and morning. If the skin should seem* inflamed and sensitive, 1 per cent. sulphur-salicylic can be used in zinc paste, or calamine liniment prescribed. Occasionally psoriasi form eruptions resist these remedies, but yield to 1 per cent. crude tar paste or to quinolor ointment in equal parts of soft paraffin. Baths containing weak potassium permanganate solution do no harm, may do some good and seem to impress th patient

General Treatment

It has been stressed by Ingram that the seborrhoeic subject is not just an individual with a greasy skin, but a person often subject to chronic infective states of the mucous membranes, with a tendency to gastro-intestinal disorders, malnutrition and nervous *instability*

There is no doubt that hidden *foci of sepsis* are often found in these patients, and elimination of these is not infrequently followed by great improvement of the skin. X-ray *examination of* the teeth and sinuses is indicated in many cases, and the possibility

of focal sepsis from such organs as the gall-bladder urinary bladder and prostate should not be forgotten.

Any treatment which improves the general health is worth consideration, such as a course of general ultra-violet light or a long holiday spent in the open air and sunshine. A careful history will show that many of these patients have had gastric symptoms at one time or another often in the nature of a vague dyspepsia but not infrequently the diagnosis of duodenal ulcer has been considered and the patient fully investigated for this.

During the past hundred years, many physicians have come to the conclusion that a seborrhoeic dermatitis is often associated with some dietetic deficiency for instance Tilbury Fox says "This cell proliferation is an evidence of a somewhat lower type of vitality and implies nutritive debility This may be the result of hereditary peculiarity and it is certainly evoked by irritants of all kinds acting upon a debilitated system." To this day many dermatologists feel that the key to the prevention of this disease lies in an adequate diet, and for a time it was thought that the administration of vitamin B complex might be the answer Unfortunately this has not proved to be the case but some patients are greatly helped by large doses of the complex given by mouth, but more often by the injection of a crude liver extract such as Campolon (Bayer) once a week for four to six doses Recently Andrews, Post and Domonkos* have advocated vitamin B and B concentrate by injection, in a dosage of 10 to 30 micrograms once a week or a fortnight, and have claimed outstanding successes. These results have not been confirmed, but there is no doubt that some patients respond extremely well to this therapy though others do not improve in the least. I have, however found it of great value in small children with particularly obstinate flexural lesions, as rapid healing often occurs after failure of all other methods with the administration by mouth of Cytacon (Glaxo) one to two teaspoonfuls thnce daily (i.e 25 micrograms thrice daily)

The value of a diet low in carbohydrates and fats and high in proteins has been advocated particularly by Barber* who recommends an anti-retentional diet and restricted fluid intake. These patients usually are fond of a sweet starchy diet, and tend to enjoy artificially prepared foods, rather than fresh country products.

A few cases which can be labelled clinically seborrhoeic dermatitis have close affinities with the asthma-eczema syndrom_, and

respond to appropriate treatment, such as a change of climate or a diet designed to eliminate specific sensitivity to foods.

The individual should be encouraged to live a less sedentary life to wear less, thinner and softer clothing and to take a cold bath or shower daily Soap and water are not contra-indicated, unless there is notable eczematization, and daily washing followed by a thorough dusting with talcum powder is advisable for flexural dermatitis. Medicated soaps have proved to be no better and no worse than ordinary toilet ones.

It must not be forgotten that people with a tendency to seborrhoeic dermatitis are probably the most liable to severe drug reactions such as are provoked by sulphonamides and the antibiotics. Therefore these must be used only if there are strong indications and under careful supervision. There is no doubt but that excellent results are sometimes obtained in patients in whom pyoderma is excessive, but these are the very ones most liable to reactions. The sulphonamides are rarely used nowadays but penicillin aureomycin and terramycin have their definite place in therapy

Despite the part endocrines play in precipitating attacks of seborrhoeic dermatitis, they are of little value in treatment. Though one might expect oestrin preparations to be useful in lesions occurring in women after the menopause, the effects are almost invariably disappointing Occasionally thyroid extract in small doses seems to have a good action in obese patients.

Vaccines and non-specific protein shock therapy have had their advocates but seldom are to be recommended The same applies to psychotherapy as a rule more help can be given to these patients by a sensible wordly wise general practitioner than by the average psychiatrist.

3 POSSIBILITIES OF SPECIFIC THERAPY IN BACTERIAL ECZEMA

H STORCK

By bearing in mind the primary or secondary part played by bacteria in the pathogenesis of eczema one may sometimes obtain surprising and permanent therapeutic successes this applies particularly to relapsing cases with marked sensitivity to the organisms which are present in the lesions in great numbers Thus in cases

investigated bacteriologically one could demonstrate a close correlation between therapeutic success following parenteral and topical penicillin, and the sensitivity to this antibiotic shown by the eczema producing organisms (Storck and Rinderknecht[7]). Therapeutic success was not usually obtained, however when gram-negative bacilli (which usually produce penicillinase) were found along with penicillin sensitive staphylococci. Recently success with the newer antibiotics, such as aureomycin, chloromycetin and terramycin has not been subject to interference by this type of enzyme and hence they have produced better results than penicillin. Cases of contact sensitization to the newer antibiotics are also far less frequent.

Dermatologists have for many years known empirically that anti-bacterial remedies are, on the whole, useful in the treatment of eczema, hence bactericidal agents, such as metallic salts, organic dyes and dilute antiseptics, were often incorporated in ointments, shake lotions and compresses. Frequently however dramatic initial improvement was followed by a stationary or even relapsing phase, in spite of continuing with anti-bacterial treatment; this was the result of primary and secondary allergic effects (*e.g.* to the topical applications) increased bacterial resistance and endogenous, constitutional factors.

Specific therapy in the form of vaccine injections, given subcutaneously in increasing dosage, has often been used, in particular those organisms recovered from the skin or their metabolic products have been employed in this way with the object of *producing* desensitization or an increased immunity. Such vaccines are usually injected subcutaneously once to three times weekly in ascending doses, for a prolonged period, local or general reactions are an indication for reducing the dosage. The effect of this treatment is difficult to evaluate in view of the unpredictable behaviour of chronic, recurrent eczema and of the effects of local treatment used at the same time. Nevertheless we saw twenty-two successful results in sixty-nine cases of chronic, recurrent eczema in which bacterial flora were obviously playing a part; these cases were treated with vaccines for weeks or months and followed up for one or two years. As mentioned in Chapter VII reactions of varying intensity occurred sixteen times; these took the form of a flare-up at the primary focus, more rarely the appearance of dissemination, and in two cases the appearance of erythema nodosum which, in one instance, undoubtedly indicated the lighting up of a tuberculous peritonitis. In one case a first attack of psoriasis was provoked.

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Complications such as these indicate that vaccine therapy should be used with caution

As regards the reactivity of the skin to bacteria vaccine injections served to reduce the epicutaneous reaction in seven instances and the reaction to intradermal injection of filtrate in eleven Therapeutic success seemed to be independent of any alteration produced in cutaneous sensitivity

According to Colebrook and others (cited) normal skin has the property of disinfecting itself of surface organisms such as haemolytic streptococci *Staphylococcus aureus* and coliform bacilli One could therefore suspect that persons subject to bacterial eczema would show a reduction of self-sterilization By infecting normal and eczematous skins and then studying the phenomenon of self disinfection we were able to show that this varies greatly from time to time: repeating the same studies before and after vaccine therapy we were unable to demonstrate definite changes in self-sterilizing power Attempts to measure changes in resistance to cutaneous bacteria produced by vaccine therapy for instance by studying the bactericidal power of serum and citrated blood, were also unsuccessful Here too extremely wide variations were found in the same patient at different times: the bactericidal power of control sera was not greater than that of the serum of eczema patients: and particularly no specific rise in the bactericidal power of the serum could be shown after vaccination

4. PRACTICAL MANAGEMENT OF NON ATOPIC ECZEMA

L J A. LOEWENTHAL

The general principles laid down in Chapter XII together with the foregoing specialized contributions, should almost enable the reader to undertake the rational management of any eczema Three essentials must, however be borne in mind first that no systemic or topical therapy can take the place of aetiological approach and management; secondly that general principles are of first importance while detailed measures are being considered and thirdly that non-atopic eczema includes an extremely high proportion of cases of contact eczema Many authorities believe that a far larger number of these will develop an allergic sensitivity to many of our most useful topical remedies hence anaesthetics such as benzocaine, anti-histaminics, sulphonamides penicillin and mercury must be

applied only for short periods or not at all. For the same reason any other potentially allergenic substance should be incorporated in ointments or creams with reluctance and only when the patient is under supervision, for sensitivity to topical medicaments occurs most frequently when these vehicles are used.

The first essential in topical therapy is the choice of the correct vehicle: this has been touched on before, but it cannot be repeated too often. The correct application for acutely inflamed, weeping areas is the cold compress (Prescriptions 1-4) followed, when there is little or no exudation, by a mild dusting powder (Prescription 7). A watery tincture is often preferable to the direct change to a shake lotion (Prescriptions 15-17) and Nos. 30 and 31 can be used at this stage. As a rule all these are well tolerated, but when the stage of occlusive vehicles (pastes, creams and ointments) is reached a preliminary trial on one or two small areas may be made. Pastes should be used in preference to ointments if there is any doubt as to a greasy base being tolerated. When possible I prefer a paste to be bandaged on under a linen strip for twenty-four hours at a time, and discourage attempts at vigorous removal between dressings. The prescriptions given by Witten and Sulzberger in Appendix B amply cover the requirements of nearly all types of eczema. The two exceptions I have in mind are:—

1. **Xerotic and Winter Skins.** These often react badly to ointments made with the vehicles suggested in the Formulary. In such cases the use of an animal fat may produce excellent results and adeps lanae hydrosa is suitable; for ease of application this can be thinned with olive oil and secondary infection controlled with an antiseptic (Prescription 32). If a paste is indicated in such cases adeps lanae may be substituted for mineral grease.

2. **For Dry Infected Lesions** (erythemato-squamous, parakeratotic and dry seborrhoeic eczema) in situations where pastes can conveniently be used I have had success with Prescription 33.

The table does not pretend to give more than a guide to the type of treatment applicable to the chief varieties of eczema. The dermatologist's early training and experience have taught him that different parts of the body's surface require different types of application, thus the axillae and groins do not usually tolerate ointments and pastes; the eyelids and the front of the neck cannot stand the same concentration of a remedy as, for instance, the scalp and limbs. Such fundamental principles are not within the scope of this work and a modicum of basic training has to be assumed.

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4 PRACTICAL MANAGEMENT OF NON ATOPIC ECZEMA

L. J A. Loewenthal

The general principles laid down in Chapter XII together with the foregoing specialized *contributions, should almost enable the* reader to undertake the rational management of any eczema Three essentials must, however be borne in mind. first, that no systemic or topical therapy can take the place of aetiological approach and management; secondly that general principles are of first importance while detailed measures are being considered and thirdly that non-atopic eczema includes an extremely high proportion of cases *of contact* eczema Many authorities believe that a far larger number of these will develop an allergic sensitivity to many of our most *useful topical remedies* hence anaesthetics such as benzocaine, anti-histaminics sulphonamides, penicillin and mercury must be

4 Chronic ( ) localized	Sulphapyridine (prolonged)* Arsenic	1–, 13 8, 33 (if infected) Fractional X-ray therapy (72 weekly) Thorium-X in alcohol	5 non-alkaline detergents, benzene, ether	Stop X-ray and greasy applications if dissemination threatens
(b) generalized	Cortisone or ACTH t procure temporary remissions Sulphapyridine (prolonged) Arsenic	11 Fractional X-ray therapy not more than 25% of body surface at each sitting	Non-alkaline detergents	—
5 Erythemato-squamous (infective)	Antibiotics in severe cases	8, 9 14A, 14B, 33 32 (if on xerotic winter skin ")	1* Cetavlon soln or non-alkaline detergents	—
6. Hypostatic	Antibiotics when indicated by lymphangitis or cellulitus	Depending on whether chemical or infective. Zinc-gelatine bandage for underlying congestive state when skin can tolerate.	35 or 1% Cetavlon soln	Watch for dissemination

These drugs have not been subjected to extensive trials outside South Africa. It is possible that the reader will prefer to omit their use and rely on harmless but probably inactive therapy with calcium and oral anti-histaminics.

TABLE X

GUIDE TO TREATMENT OF NON-ATOPIC, NON-SEBORRHOEIC ECZEMA

TYPE AND STAGE OF ECZEMA	SYSTEMIC THERAPY	TOPICAL APPLICATIONS	TYPE OF CLEANSING (When necessary)	PRECAUTIONS
1 Acute contact eczema (a) weeping and crusted	Cortisone or ACTH for 1 week	Prescriptions 1 2, 3 35	35	—
(b) erythematous and papular or papulo-vesicular	Cortisone or ACTH for 1 week	Prescriptions 1 2, 3 followed by 7 or 30, 31	Bathing with 1 2, 3	—
(c) grossly infected	Antibiotics if systemic signs are evident	Prescriptions 1 – 3 followed by 34	35 or 1% Cetavlon soln.	Watch for silent systemic infection if cortisone or ACTH is being given
– Acute disseminated or endogenous	Cortisone or ACTH for 1 weeks Sodium p-aminobenzoate for 1 week	Prescriptions 1 – 3 followed by 7 or 30, 31	3/AS BATH	Attention to primary focus: no X ray no occlusive dressings
3 Subacute (?-4 weeks) disseminated or endogenous ( ) erythematous or papular	Cortisone or ACTH for 1 2 weeks Sulphapyridine	Prescriptions 15 16, 17 Sub-fractional X-ray therapy (38) twice weekly	1 – 3 or 1% Ceta lon soln.	As above
(b) Infected	Sulphapyridine* Antibiotics f systemic signs re evident.	Prescriptions 34 33	2, 3 35 or 1% Ceta lon soln.	A hove

Appendix A

TABLE OF CONCENTRATIONS AND VEHICLES TO BE USED IN PATCH TESTING‡

KEY TO ABBREVIATIONS AND SYMBOLS

acet.	= acetone	pet.	= petrolatum
alc.	= alcohol 70 per cent.	prop.	= proprietary preparation
aq.	= aqueous	sat.	= saturated
chlor	= chloroform	sol	= solution
c	= castor oil		
controls	= perform control tests on normal subjects		
dext.	= 15 per cent. dextrose solution		
o.	= olive oil		
pdr	= powder		

We suspect that the concentration given is too strong for routine testing.

† This substance has been known t cause sensitization of the eczematous type, even after single application to normal skin.

Substance		Dilution (per cent.)	Vehicle
Acetanilid	pdr	as is	
Acetic acid		3	aq
Acetone		as is	
Acetphenetidin	pdr	as is	
Acridine	pdr	pure	
Alcohol, denatured		as is	
Aldehyde ammonia		as is	
Alizarin		pure	
Alizarin 778		1	lc.
Alizarin red 1014	pdr	as is	
Alizarin sulphate		10	aq
Alkaloids, as salts		1	aq
Allspice		as is	
Almond oil		as is	
Alpha naphthylamine		pure	
Alum		10	aq
Aluminium scrapings		as is	
Aluminium acetate		10	aq
Aluminium chloride			aq
Alypin			aq.
Amber oil of		1	aq
Amido-azobenzol		1	alc.
Amido-azotoluene hydrochloride		10	o.o
Amidol		1	aq
Amidophenol (ortho, meta or para)		5	aq
Amidopyrin		10	pet
Amines		as is	
Amino-azotoluene		2	pet.
Amino-azotoluene		2	alc.
Aminodacrylic acid	pdr	as is	
Ammonia		1	alc.
		1 2	aq.

‡ Adapted from "Allergy" by E. Urbach and P. M. Gottlieb (Wm. Heinemann Medical Books Ltd 1946.)

Again many patients are seen only when they are already suffering from the effects of mismanagement. In such cases additional caution is required "promotion" from compresses, powders and shake lotions to pastes, creams and ointments must be undertaken with more than the usual caution and even routine remedies must first be tested on limited areas

It is a sad but true reflection that most patients with a chronic eczematous eruption do not dare to hope for a cure; they do not, however expect to be made worse. It would be idle to pretend that the treatment of eczema is wholly satisfactory Much remains to be learned and much, no doubt, to be unlearned. Yet for the *practitioner who has mastered the essentials of therapy* and who *is willing to devote time and trouble to his cases the rewards are rich indeed.*

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PATCH TESTING—*continued*

Substance		Dilution (per cent.)	Vehicle
Beeswax		pure	
Benzaldehyde		10	aq
Benzanthrone		pure	
Benzidine		pure	
Benzene		60	o.o.
Benzocaine		5	pet.
Benzoic acid		6	pet.
Benzoic anhydride		10	aq.
Benzol		60	o.o.
Benzoquinone		1	aq
Benzoyl amino-metoxychlor anthraquinone		2	o.o
Benzyl alcohol		10	pet.
Benzyl benzoate		10	aq.
Benzyl chloride		5	aq.
Benzyl cinnamate		10	pet
Bergamot, oil of		10	pet.
Betahydroxy anthraquinone		1	alc.
Betanaphthol		10	o.o
Beta phenylacrylic acid		5	pet.
Bismarck brown-331		pure	
Bismogenol		as is	
Bismuth, colloidal solution		as is	
Bismuth oxychloride		5	pet
Bismuth subgallate		pure	
Bismuth subnitrate		.5	pet
Bismuth subsalicylate		14	o.o.
Black flag (prop.)	pdr	as is	
Black flag (prop.)	liquid	.5	
Black rouge		as is	
Bleaching powder (controls)		10	aq
Bluing		as is	
Borax		sat. sol	
Boric acid	pdr	pure	
Boric acid ointment, U S P		as is	
Borocaine (procaine borate)		1	aq
Brake fluid (prop.) (controls)		as is	
Brass, metallic scrapings		as is	
Brass weldings, scrapings		as is	
Brass polish		10	aq
Brazil ood (redwood)		as is	
Brazil nut		as is	
Brilliant cresyl blue BB(L) 877		pure	
Bromo acid 768		pure	
Bronze liquid paint		as is	
Burow solution (liq. alum. acet.)		10	aq
Butesin		1	alc.
Butesin picrate ointment (prop.)		as is	
Butyl acetate		pure	
Butyl alcohol		pure	
Butyric acid		1	aq.
Cade, oil of		5-10	pet.
Cadmium orange		pure	
Cadmium red, deep		pure	
Cadmium red, light		pure	
Caffeine		1	aq
Calamine		as is	
Calcium arsenate	pdr	pure	

PATCH TESTING—*continued*

Substance		*Dilution (per cent.)*	*Vehicle*
Ammonium bichromate		0·5	aq.
Ammonium bichromate		0·5	pet.
Ammonium carbonate		15	aq
Ammonium chloride		3	aq.
Ammonium fluoride		0·5	aq
Ammonium nitrate		*10*	aq
Ammonium persulphate		1·5	aq.
Ammonium sulphate		10	aq
Amydricaine hydrochloride		1	aq.
Amyl acetate		pure	
Analgesics		as is	
Anesthesin		5	pet
Aniline		10–25	o.o.
Aniline black 870	pdr	pure	
Aniline brilliant green	pdr	pure	
Aniline dyes			o.o.
Aniline dyes		2	pet
Aniline dyes	pdr	pure	
Anise seed oil		25	c.o.
Anthracene		pure	
Anthralin (1,8-dihydroxyanthranol)		0·1	pet.
Anthraquinone, powder		pure	
Anthraquinone blue S.R. 1089		pure	
Anthrarobin		3	pet.
Antihidrotics (prop.) (controls)		as is	
Antimony chloride			aq
Antimony oxide		pure	
Antipyrine		as is	
Aquaphor (prop.)		as is	
Arachis oil		as is	
Argyrol		10	aq
Arnica, tincture of		20-25	pet.
Arnica, tincture of		20-25	alc.
Arning's tincture, modified (anthrarobin, tumenol, glycerin, spirits, ether)		as is	
Aromatic oils		1	alc.
Arsenious trioxide	pdr	pure	
Asphalt (no adhesive covering)		as is	
Aspirin		as is	
Atropine sulphate		1	aq
Auto lubricating oils		60	o.o.
Auto polishes (controls)		as is	
Azochloramid		0·2	*triacetin*
Bakelite (scrapings)		as is	
Baking powder		as is	
Baking soda		as is	
Balata (rubber)		as is	
Balsam of Peru		10	pet.
Banana peel oil		pure	
Barbiturates		as is	
Barium hydrate		0·5	aq
Barium sulphate		as is	
Barley oil		pure	
Bayberry oil of		25	o.o
Bayberry oil of		25	pet
Beef fat oil		pure	
Beef salt		5	aq

PATCH TESTING—*continued*

Substances		Dilution (per cent)	Vehicle
Beeswax		pure	
Benzaldehyde		10	aq
Benzanthrone		pure	
Benzidine		pure	
Benzine		60	
Benzocaine		5	pet.
Benzoic acid		6	pet.
Benzoic anhydride		10	aq.
Benzol		60	o.
Benzoquinone		1	aq.
Benzoyl amino-metoxychlor anthraquinone		2	o.o
Benzyl alcohol		10	pet.
Benzyl benzoate		10	aq.
Benzyl chloride		5	aq.
Benzyl *cinnamate*		10	pet
Bergamot, oil of		10	pet
Betahydroxy anthraquinone		1	alc.
Betanaphthol		10	o.o
Beta-phenylacrylic acid		5	pet.
Bismarck brown-331		pure	
Bismogenol		as is	
Bismuth, *colloidal solution*		as is	
Bismuth oxychloride		5	pet
Bismuth subgallate		*pure*	
Bismuth subnitrate		25	pet
Bismuth subsalicylate		14	o.
Black flag (prop.)	pdr	as is	
Black flag (prop)	liquid	25	o.
Black rouge		as is	
Bleaching powder (controls)		10	aq
Blueing		as is	
Borax		sat. sol	
Boric acid	pdr	pure	
Boric acid ointment, U.S.P		as is	
Borocaine (procaine borate)		1	aq
Brake fluid (prop) (controls)		as is	
Brass, metallic scrapings		as is	
Brass weldings, scrapings		as is	
Brass polish		10	aq.
Brazil wood (redwood)		as is	
Brazil nut		as is	
Brilliant cresyl blue BB(L) #77		pure	
Bromo acid 768		pure	
Bronze liquid paint		as is	
Burow solution (liq. alum. acet.)		10	aq
Butesin		1	alc.
Butesin picrate ointment (prop.)		as is	
Butyl acetate		pure	
Butyl alcohol		pure	
Butyric acid		1	aq.
Cade, oil of		5-10	pet.
Cadmium orange		pure	
Cadmium red, deep		pure	
Cadmium red, light		pure	
Caffeine		1	aq.
Calcamine		as is	
Calcium arsenate	pdr	pure	

PATCH TESTING—*continued*

Substance		*Dilution (per cent.)*	*Vehicle*
Calcium carbonate		3	aq
Calcium chloride		10	aq
Calcium cyanamide (crude)		10	aq
Calcium fluoride		0·5	aq
Calcium hydrate		0·1-·5	aq.
Calcium nitrate		10	aq
Calcium oxide		10	aq
Calcium phosphate		10	aq.
Calcium sulphide		1	aq
Calmitol ointment (prop.)		as is	
Calomel	pdr	pure	
Camomile, oil of		·5	c.o.
Camomile oil of		25	pet.
Camphor	pdr	pure	
Camphor ice (prop.)		as is	
Camphor oil of		10	pet.
Camphor spirits of		as is	
Canada balsam		as is	
Cantharides, tincture of		1	alc.
Capsicum, tincture of		1	alc.
Caraway seed, oil of		·5	c.o.
Caraway seed, oil of		1	alc.
Carbazole	pdr	pure	
Carbon		as is	
Carbon disulphide		60	o.o.
Carbon paper		as is	
Carbon tetrachloride		pure	
Carborundum		as is	
Cardamon		as is	
Cashew nut shell oil		3-5	alc.
Cassia, oil of		1	alc.
Cement (controls)		as is	
Cerealn		pure	
Cetaceum		pure	
Charcoal		as is	
Chestnut, extract of		10	aq.
Chicken fat oil		pure	
Chinosol (pot. hydroxyquinolin. sulph.)		0·-0·5	dext.
Chloral hydrate		10	aq
Chloramine		0·5-1	aq
Chlorbenzene		5	o.o.
Chlorbutol			alc
Chlorinated lime		10	aq
Chlorinated naphthaline		pure	
Chloroform		40	o.o.
Chocolate		as is	
Chrome alum		as is	
Chromic acid		0·5-1	aq
Chromium chloride			aq
Chromium potassium sulphate		10	aq
Chromium sulphate		2	aq.
Chrome yellow	pdr	pure	
Chrysarobin		1·5	pet.
Chrysoidin brown	pdr	pure	
Cinnabar		3	pet.
Cinnamic acid		5	pet.
Cinnamon	pdr	as is	

PATCH TESTING—*continued*

Substance	*Dilution (per cent.)*	*Vehicle*
Cinnamon, oil of	5	o.o.
Cinnamylic acid	5	pet.
Citric acid	1	aq.
Citronella	as is	
Cleaning fluids, non-inflammable (prop.) (controls)	as is	
Cleaning fluids, inflammable (prop.) (controls)	60	o.
Clothing and clothing materials	as is	
Cloves pdr	as is	
Cloves, oil of	25	o.o.
Cloves, oil of	1	alc.
Coal tar crude	5-10	pet.
Cobalt chloride	2	aq
Cobalt oxide	pure	
Cocaine	1	aq.
Cochineal natural-932	10	aq
Cocoa	as is	
Coconut, oil of	pure	
Codeine sulphate	1	aq
Cod fish oil	pure	
Cod liver oil	as is	
Coffee	pure	
Coffee, oil of	pure	
Collodion	as is	
Colza oil	as is	
Copal	pure	
Copper chloride	1	aq.
Copper cyanide pdr	pure	
Copper scrapings	as is	
Copper sulphate	5	aq
Coriander oil of	1	alc.
Cosmetics (controls with hair tonics, etc cuticle softeners, et are usually primary irritants)	as is	
Cotton seed oil	pure	
Crayons	as is	
Creosote	10	o.o.
Cresol	0 5-1	aq.
Crude oil	as is	
Crystal violet 681	2	aq.
Cumaron	pure	
Cutch	pure	
*Cuticle remover (controls)	as is	
Cyclohexanol	50	o.o.
Dammar (resin)	pure	
Decahydronaphthalene (dekalin, turpentine substitute)	50	o
Denatured alcohol (controls)	as is	
Deodorants	as is	
Depilatories (controls)	as is	
Dermatol (prop dusting powder)	as is	
Dextrins	pure	
Diacetylaminoazotoluol	50-80	aq
Diamidines		pet.
Diazonium salts	pure	
†Di-beta-naphthyl-paraphenylene-diamine	1	pet.
†Dichlorbenzene	pure	
Dichlorbenzidine	5	chlor
Dichloroacetic benzene	5	alc.
	10	aq.

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PATCH TESTING—*continued*

Substance		*Dilution (per cent.)*	*Vehicle*
1 2-4 dichloronitrobenzene		1	acet.
1-4-2 dichloronitrobenzene		1	acet.
Diethylanius-ethanol		1	aq
Diethylene glycol		10	aq
1-8 dihydroxy-anthranol		0·1	pet
1 2 dihydroxy-anthraquinone		0·5	alc.
1-8 dihydroxy-anthraquinone		0·5	alc.
1-4 dihydroxy-anthraquinone		0·5	alc.
Dimethyl amine		pure	
Dimethyl aniline		10-.5	o.o.
†1 2-4 dinitrochlorbenzene		1	acet
Dinitrocresol		5	chlor
-4 dinitrophenol		10	aq
Dinitrotoluol		sat	alc.
Di-orthotolyl guanidine	pdr	pure	
Di-orthotolyl thio-urea	pdr	pure	
Diphenyl		pure	
Diphenyl-guanidine		2 10	o.o
Dithio acids, salts of		pure	
Dithranol		3	pet
Ditolyl amines		pure	
Dragon's Blood		as is	
Dusts		as is	
Dust oil		as is	
Dutch Cleanser (prop.)		as is	
Dyes, lakes and toners	pdr	pure	
Earthy pigments		pure	
El Key " Insecticides (prop.)		50	o.o
Emetine hydrochloride	pdr	pure	
Enamel (controls)		as is	
Eosin	pdr	as is	
Ephedrine		1	o.o
Erythrosin		as i	aq
Esbach's reagent		1	alc.
Essential oils (controls)		pure	
Esters		pure	
Ester gums		60	o.o
Ether		pure	
Ethyl acetate		50	o.o
Ethylene d chloride		0 1	alc.
Ethylene dichloride		0 5	aq
Ethyl mercury chloride		0·5	aq
Ethyl mercury phosphate		1	alc.
Eucalyptus, oil of	pdr	pure	
Euflavine		as is	
Eye lotions, cosmetics, shadows		5	pet
Fagi, oil of		pure	
Fenchyl alcohol		1	alc.
Fennel, oil of		2	aq.
Ferric chloride		as is	
Ferric ferrocyanide		10	aq
Ferric sesquichloride		10	aq
Ferrosulphate		as s	
Fertilizers, most commercial preparations (controls)		as i	
Fixative		2	alc
Flavouring oils (controls)		25	o.o
Flit (prop.)			

PATCH TESTING—*continued*

Substance	Dilution (per cent.)	Vehicle
Floor wax (controls)	10	o.
Flour all kinds	as is	
Flour bleaches (controls)	as is	
Flowers, fresh, dry artificial (controls)	as is	
Fluorescein	1	alc.
Flux, aluminium	as is	
Flux, iron	as is	
Flycide (prop.)	5	o.o.
Foods, any kind (except rinds of certain fruits, spices, mustard, etc.)	as is	
Formaldehyde	5	aq.
Formic acid	1	aq.
Fowler solution (liq. arsenicalis)	as is	
Fruit, citrus, peel (controls)	as is	
Fuchsin	10	aq
Furfural	pure	
Furniture polish (controls)	10	o.o.
Furs, any, dyed, natural	as is	
Fustic (yellow wood)	pure	
Fustic (yellow wood)	sat.	aq.
Gallalith	as is	
Gasoline, ordinary, ethyl	60	o.
Gentian violet (BDC) 600	2	aq
Ginger pdr	pure	
Ginger, oil of	25	c.o.
Glue	as is	
Glycerine	pure	
Glycerine oil	as is	
Glyptal (prop.)	pure	
Gold Dust (prop.)	as is	
Gold sodium thiosulphate	0·5	aq.
Grapefruit peel oil (controls)	pure	
Graphite	as is	
Greases	as is	
Grease solvents, most proprietaries (controls)	as is	
Guanidines	pure	
Gum arabic	as is	
Gun grease	as is	
Gun powder	as is	
Gutta-percha	as is	
Gutta [illegible] (rubber)	as is	
Hair, all kinds, natural, dyed	as is	
Hair dyes	as is	
Hair lacquers	as is	
Hair tonics, lotions (controls)	as is	
Hat glazing, sizing or lacquers for (controls)	as is	
Hempseed oil	as is	
Henna, Egyptian	as is	
Henna, white	as is	
Hexahydrophenol	as is	
Hexalin ($C_6H_{11}OH$)	50	o.o.
Hexamine	50	o.o
Hexylresorcinol	pure	
Histamine (acid phosphate)	as is	
Homatropine	0·1	aq
Hydrochloric acid	1	aq
Hydrofluoric acid	1	aq
	0·2	aq.

PATCH TESTING—*continued*

Substance	*Dilution (per cent.)*	*Vehicle*
Hydrogen sulphide	10	aq.
Hydroquinone	5	aq
Hydroterpens	50	o.o.
Hydroxymercurichlorphenol	0·5	aq.
Hydroxymercuricresol	0·5	aq
Hydroxymercurinitrophenol	0·5	aq
Hypnotics	as is	
Ichthammol	5 10	pet.
Indigo	10	aq.
Indole	sat.	aq
Inecto A (prop. hair dye)	as is	
Inecto B (prop hair dye)	as is	
Ink eradicators (controls)	as is	
Inks	as is	
Iodine crystals	0·5	pet.
Iodine crystals	1	alc.
Iodine, tincture of U.S.P (do not cover! simply paint on)	as is	
Iodobismitol (prop)	as is	
Iodoform	25	pet.
Iridium chloride	10	aq
Iron chloride		aq
Iron metallic scrapings	as is	
Iron sulphate	10	aq
Istizin 1-8 dihydroxy-anthraquinone	0·5	alc.
Javelle water	10-20	aq
J O Roach Powder (prop. insecticide)	as is	
Juniper oil of	25	c.o.
Juniper oil of	1	alc.
Kainit (prop. fertilizer)	10	aq
Karbolinum (prop wood preservative)	50	o.o
Kerosine	60	o.o.
Kill It (prop insecticide)	as is	
Lac dyes	50	pet.
Lacquers (controls)	as is	
Lakes	50	o.o.
Laketine pdr	as is	
Lanolin (wool fat)	as is	
Lard	as is	
Larocaine (prop)	1	aq
Latex	as is	
Laurel, oil of	–5	c o.
Lavender oil of	1	alc
Lead, white	as is	
Lead, red	as is	
Lead arsenate	pure	
Lead arsenate	5	aq
Lead azide	pure	
Lead chloride	pure	
Lead styphnate	pure	
Lead subacetate	0-	aq
Lead sulphide		aq
Leathers, natural, tanned, dyed, imitation	as is	
Lemon oil of (*control*)	1	alc
Licorice	as is	
Lime, burnt	10	aq
Lime, slaked (controls)	as is	

PATCH TESTING—*continued*

Substance	*Dilution (per cent.)*	*Vehicle*
Linalool	1	alc.
Linseed oil	as is	
Lipstick	as is	
Liquor carbonis detergens	10	pet.
Liquor sesquichlorati	10	aq.
Listerine (prop.)	10	aq.
Lithol red 189 as lakes and toners	as is	
Logwood	sat.	aq.
Lubricating oils (controls)	as is	
Lugol' solution, U.S.P.	50	aq.
Lusoform (prop.)	as is	
Lysol (prop.)	1	aq.
Mace, oil of	1	alc.
Machine oil (controls)	50	o.o.
Manganese oxide	pure	
Maroon 677 (partly *impure magenta*)	as is	
Mascara	as is	
Mastic	pure	
Mastisol (prop. collodion-like substance)	as is	
Melissa, oil of	1	alc.
Menthol	1	pet.
Mentholatum (prop.)	as is	
Mercaptans	pure	
Mercurochrome	2	aq.
Mercury bichloride	0·1	aq.
Mercury fulminate	pure	
Mercury oxycyanate	0·1-0·2	aq.
Mercury white ammoniated	5-10	pet.
Mercury yellow oxide of	5	pet.
Merthiolate, *tincture of* (prop.)	as is	
Mesquite wood	as is	
Metals, pure, alloys	as is	
Metaphen (prop.)	0·5	alc.
Metatoluylene diamine	pure	
Methol (prop.)	5	aq.
Methyl acetate	pure	
Methyl alcohol	pure	
Methyl aniline	10-25	o.o.
Methyl benzoate	1	aq.
Methyl heptin carbonate	0·1	alc.
Methyl orange 142	5	aq.
Methylprotocatechuic aldehyde (vanillin)	10	pet.
†Methyl salicylate	2	
Methyl violet-680	2	aq.
Methyl violet, as lake	as is	
Michler hydrol	5	alc.
Mineral colours or pigments	as is	
Mineral oil	as is	
Mica	as is	
Mirbane oil (nitrobenzene)	25	o.
Mitol (prop.)	as is	
Monobenzyl-para-amino phenol	pure	
Monochlor-benzene	5	
Morphine	1	aq.
Moth flakes	as is	
Mouth washes	as is	
Mucilage	as is	

PATCH TESTING—*continued*

Substance	*Dilution (per cent)*	*Vehicle*
Mustard, oil of	1	alc.
Naftalan (prop.)	10	pet.
Nail polish	as is	
Naphtha	50	o.o.
Naphthalic acid	1 5	aq
Naphthalene	pure	
Naphthalene-1-sulphonic acid azo-beta-naphthol	as is	pdr
Naphthenol	50	o.o.
Naphthol yellow	pure	
Naphthylamine		alc.
Neoarsphenamine	1	aq
Nickel nitrate	5	aq
Nickel sulphate	5-10	aq.
Nicotine salicylate	5	aq
Nigrosin	pure	
Nile blue	pure	
Nitric acid	2 3	aq
Nitrobenzene	10-.5	o.o
Nitrophenol	5	chlor
†Nitroso-dimethyl aniline	1	alc.
Novocain (prop.)	2	aq.
Nupercaine (prop.)	1	pet.
Nutgalls, roasted	as is	
Nutmeg, oil of	.5	c.o.
Nylander's reagent	as is	
Nylon	as is	
Oakum	as is	
Oat oil	as is	
Ochre red	pure	
Oidiomycins (controls)	undil.	
Oil of bitter almonds	1	alc.
Oil paints, in tubes	as is	
Oil paints, for walls	50	o.o.
Olibanum	*pure*	
Olive oil	pure	
Orange, oil of	.5	c.o.
Orange, oil of	1	alc.
Orange II 151 as lake	pure	
Orris root, powder	pure	
†Orthocain	.5	pet.
Orthonitranisol	5	aq
Osmic acid	10	aq
Oxalic acid	5	aq
Paint, house	50	o.o.
Palladium chloride	10	aq
Palm oil	as is	
Panthesin	1	aq
Para-amidophenol	3	aq
Para-amidophenol	10	o.o
Para-aminodiphenyl amine	3	aq
Para-aminophenol	10	pet.
Para-di-chromo benzine	10	aq
Paraffin	pure	
Paranitro benzoic acid	pure	
Paranitrochlorbenzene	10	acet.
†Paranitroso-dimethylaniline	1	acet
Paraphenylenediamine		pet

PATCH TESTING—*continued*

Substance	*Dilution (per cent.)*	*Vehicle*
Para red, deep-44, as ink or toner	as is	
Para red, light-44 as ink or toner	as is	
Pastes	as is	
Peanut oil	as is	
Pelodol (prop.)	2	pet.
Peppermint, oil of	25	c
Peppermint, oil of	1	alc.
Perfumes (controls)	as is	
Perfume oils (controls)	1	alc.
Peroxide, U.S.P.	as is	
Persil (prop. cleansing substance)	10	aq.
Peterman's Insecticide (prop.)	25	o.
Petrolatum, white or yellow	pure	
Petroleum	20	o.o.
Phenacetin	as is	
Phenanthrene pdr	pure	
Phenazone	as is	
Phenobarbitone	as is	
Phenolphthalein, white or yellow pdr	as is	
Phenolphthalein, white or yellow pdr	2	alc.
Phenyl-alpha-naphthylamine	pure	
Phenyl-beta-naphthylamine	pure	
Phenylglycine	pure	
Phosphorus trisulphide	0·5	pet.
Photographic developers	5	aq.
Phthalic acid	1·5	aq.
†Phthalic anhydride	1	alc.
Picric acid	1·5	aq.
†Picryl chloride	1	acet.
Pigments, for artists, etc.	as is	
Pine oil (controls)	pure	
Pitch (just apply no covering)	as is	
Plant oils (commercial preps. for testing are available)	as made	
†Plants, fresh, dry any part of (controls)	as is	
Plaskon	pure	
Plaster of paris	as is	
Plaster wall	as is	
Plastics	as is	
Platinum chloride	10	aq.
†Poison ivy extract—4 per cent. solids	0·1	acet.
Polishes, commercial (prop.)	as is	
Pontachrome blue black R 202	pure	
Pontacyl black (similar to 246)	pure	
Pontamine black 581	pure	
Pontamine blue 406	pure	
Pontamine diazo black 401	pure	
Pontamine fast orange S	pure	
Pontocaine hydrochloride (butethamol)	2	o.
Poppy seed oil	as is	
Potash	10	aq.
Potassium acetate	10	aq.
Potassium arsenite, U.S.P.	as is	
Potassium bichromate	0·5-1	aq.
Potassium bromate	6	aq.
Potassium bromide	1-6	aq.
Potassium bromide	25	pet.

PATCH TESTING—*continued*

Substance	*Dilution (per cent)*	*Vehicle*
Potassium carbonate	0·7 3	aq
Potassium chlorate	10	aq.
Potassium chloride	3-10	aq
Potassium chromate	0·5	aq
Potassium citrate	10	aq.
Potassium ferricyanide	10	aq
Potassium ferrocyanide	10	aq
Potassium hydroxide	0·5	aq.
Potassium iodide	3-6	aq
Potassium iodide	5	pet.
Potassium nitrate	5	aq
Potassium permanganate	1	aq.
Potassium persulphate (should be freshly made)	5	aq
Potassium salicylate	as is	
Powder face, bath	as is	
Powder cleansing, scouring (controls)	as is	
Pragmasul oint. (prop.)	as is	
Pragmatar oint (prop)	as is	
†Primrose, expressed juice of fresh plant	5	aq
†Primrose, leaf	as is	
Procaine (base)	1	o.o
Procaine hydrochloride	1	aq
Propylene glycol	10	aq
Protein extracts, foods, plants, bacteria	as is	
Pyrethrum, milled powder	as is	
Pyrethrum, tincture of	as is	
Pyro	as is	
Pyrogallol	3	aq
Quercitron	pure	
Quinine	1	aq
Quinine sulphate	5	pet.
Quinizarin	0·5	alc.
Quinosol	0- -0·5	dext.
Rapeseed oil	pure	
Raw umber	as is	
Red moss	as is	
†Resins (controls see "Plants")	as is	
Resorcin (controls)	3	aq
Rhodamine B 749 lakes and toners of	as is	
Rhodium chloride	10	aq
Rice oil	as is	
Rockwood	as is	
Rose, oil of	5	pet.
Rose, oil of	1	alc.
Roux	as is	
Rubber rubber products	as is	
Rubber (synthetic)	as is	
Rusci oil of	6	pet.
Rye, oil of	pure	
Safranine O 841	pure	
Sagrotan (prop. disinfectant)	1	aq
Sal ammoniac	3	aq
Salicylic acid	5 10	pet
Salol	as is	
Salves (prop.) (controls)	as is	
Santal, oil of	1	alc
Sassafras, oil of		o.o

PATCH TESTING—*continued*

Substance	*Dilution (per cent.)*	*Vehicle*
Sassafras, oil of	1	alc.
Scalp lotions (controls)	as is	
Scopolamine	1	aq.
Scatol	as is	
Shampoos (controls)	as is	
Shellac (controls)	as is	
Shoe dyes (controls)	50	o.
Shoe polishes (controls)	60	pet.
Silver amalgams	as is	
Silver metallic, scrapings	as is	
Silver nitrate	5	aq
Silver nucleinate	5	aq.
Silver paint	as is	
Sunscreen (prop.)	as is	
Skatol	sat.	aq
Smokeless gunpowder	as is	
Soap, tincture of green	5	pet.
Soap, tincture of green	2·5	alc.
Soaps (controls)	1 3	aq.
Sodium arsenate	10	aq.
Sodium benzoate	20	aq.
Sodium bicarbonate	1-3	aq
Sodium bichromate	3	aq.
Sodium bromide	25	pet.
Sodium carbonate	3-10	aq
Sodium chloride	10	aq
Sodium fluoride	0·5	aq
Sodium fluorosilicate	0·5	aq.
Sodium hydroxide	0·5	aq
Sodium hypochlorite	10	aq
Sodium hyposulphite	1	aq.
Sodium meta-aminobenzoate	1	aq.
Sodium metasilicate	2	aq.
Sodium oleate	1	aq.
Sodium para-aminobenzoate	1	aq
Sodium salicylate	1	aq.
Sodium stearate	1	aq.
Sodium sulphate	5	aq.
Sodium sulphide	2	aq.
Sodium sulphite	1	aq.
Sodium thiosulphate	5	aq
Soluble blue 325	pure	
Spearmint, oil of	1	alc
Spermaceti	pure	
Spirits of ether	as is	
Spring spray (auto) (controls)	as is	
Stains	as is	
Starch	as is	
Stearic acid	1	aq
Steel wool	as is	
Sudan III, 223	5	o.
Sugar	as is	
Sulpharsphenamine	3	aq
Sulphogene carbon	pure	
Sulphogene golden brown	pure	
Sulphonamides (pdr. or 5 per cent. in cold cream, or respective topical prep. or proprietary)	as is	

PATCH TESTING—*continued*

Substance	*Dilution (per cent)*	*Vehicle*
Sulphonated oils	pure	
Sulphosalicylic acid	pure	
Sulphur (precip. or sublimed)	5-10	pet.
Sulphur monochloride	1	carb. di sulphide
Sulphur acid	5	aq
Sulphuric acid	1 2	aq.
Sulphurous acid	as is	
Sumac leaves, fresh or dry	as is	
Sunflower oil of	as is	
Tallow	as is	
Tannic acid	1	aq
Tars (no covering! simply apply)	as is	
Tar paper	as is	
Tar solution of N.F	10	aq.
Tartar emetic	3	aq
Tartar emetic, powder	as is	
Tartrazine yellow-640	pure	
Terpineol	pure	
Tetrachloronaphthalin	50	o.o.
Tetralin (tetrahydronaphthaline)	30	o.o.
Tetramethyl-diamino-benzophenone	5	alc.
Tetramethyl thiuram-disulphide	pure	
Tetramethyl-thiuram-mono-disulphide	pure	
Tetryl	sat.	ether
Thio-urea	pure	
Thiuram sulphides	pure	
Thyme, oil of	.5	c.o.
Thyme, oil of	.5	alc.
Thymol	1	pet.
Thymol iodide	25	pet.
Tin chloride (stannous)	10	aq
Tin foil	as is	
Tinctura veratri viridis, U.S.P	as is	
Tintex (prop)	as is	
Tobacco extracts (controls)	as is	aq
Tobacco leaf (controls)	as is	
Toilet waters	as is	
Toluene	50	o.o
Toluidine	10-50	o.o.
Toners pdr	pure	
Tooth pastes, powders	as is	
Tragacanth	1	aq
Triacetin	pure	
Trichlorethylene	50	o.o
Trichlortoluol	50	o.o
Trichophytins (controls)	undil	
Triethanolamine	1	aq
Trinitro-anisol	0.01	chlor
1 2-4 trinitrobenzene	1	acet.
1 3 5 trinitrobenzene	1	acet.
Trinitrophenol	1 5	aq
Trinitrotoluol	sat.	alc
Trisodium phosphate		aq.
Trypan blue 477	pure	
Trypan red 438	pure	
Tryparsamide	6	aq

PATCH TESTING—*continued*

Substance	Dilution (per cent)	Vehicle
Tuberculin (controls)	undil.	
Tumenol (prop.)	5	pet.
Tumenol ammonium (prop.)	6	pet.
Turmeric	pure	
Turpentine (controls)	50	o.
Tutocain	2	aq.
Typewriter ribbon	as is	
Tyrosine	sat.	aq.
Ultramarine blue	as is	
Uranium chloride	10	aq
Urea	10	aq
Uric acid	1	aq.
Vanilla, oil of	25	alc.
Vanillin	10	pet.
Varnish (controls)	as is	
Varnolene	60	o.o
Venetian red	pure	
Vert emeraude	pure	
Victoria blue	pure	
Vinegar	as is	
Vinyl resins	pure	
Vioform (prop.)	3	pet.
Walnut, oil of	pure	
Water colours	as is	
Wax, floor (controls)	50	o.
Waxes, polishing, in general (controls)	as is	
Wheat, oil of	as is	
Whitfield' oint., N.F	as is	
Window sprays	as is	
†Wintergreen, oil of	1	alc.
Witch hazel	as is	
Woods, natural, painted, stained (controls)	as is	
Wormwood, oil of	25	c.o.
Xeroform (bismuth tribromphenate)	25	pet.
Xylol	50	o
Yellow olive	pure	
Zinc chloride	2	aq.
Zinc oxide	pure	
Zinc peroxide	pure	
Zinc stearate	pure	
Zinc sulphate	10	aq.
Zinc white	as is	
Zonite (prop. sod. hypochlorite)	1	aq.

APPENDIX B

FORMULARY

Prescriptions 1 to 27 by WITTEN and SULZBERGER,
28 and 29 by PETERKIN
30 to 35 by LOEWENTHAL.

PRESCRIPTIONS*

1 Solution of aluminium subacetate (Liq alumini subacetatis N.F VI) or Burow's solution (Liq alumini acetatis N F VI).

Label Dilute with 15 20 parts of water and use as cleanser or apply as wet poultices or dressings.

2. Boric acid (crystals or powder)

Label ½ to 1 teaspoonful to each tumblerful of hot water allow to cool and apply as cleansing solution or as wet compress.

(Remember—as the solution evaporates the concentration of the boric acid increases.)

3 Potassium permanganate tablets 0·06 (gr j)

Label Add 1 tablet to 1 2 pints of water (1 16 000 or 1 8,000 solution) Stir and *dissolve thoroughly* before using.

4 Thiersch's solution (Liq borici salicylatis).

Boric acid	12·0
Salicylic acid	2·0
Distilled water to make	1,000·0

Label Apply undiluted as wet compresses.

5 Lubricating and softening oil

Salicylic acid	2·4 4 8
Olive oil or Liquid petrolatum to make	*240·0*

Label For softening and removal of crusts, apply as directed

6 Softening and lubricating cream and soft ointment vehicle

Liquid petrolatum	30·0
White wax	7 5
Distilled water	12·0
Sodium borate	0·225

Label Apply by gentle massage bandage on in thick layer if required

This preparation may be used also as a vehicle for antipruritics and many topical medicaments (except salicylic and other acids which will break down the emulsion).

* The National Formulas referred to in Prescriptions 1 7 are the National Formulas of U.S.A.

7 Mild dusting powder

Boric acid powder	
or Tannic acid	
or Bismuth subnitrate	1 3 3·0
Zinc oxide	
or Kaolin	
or Zinc stearate	50 0
Purified talc	50 0

Dispense in sifter top can.

Label Use freely as required.

8. Antiseptic ointment.

Neomycin sulphate	0·25 0·5
or Bacitracin	25,000 Units
or Aureomycin hydrochloride	0·25 1·5
or Terramycin hydrochloride	0·25 1·5
Vioform powder	0·5 1 5
or Ammoniated mercury	0 5 1 5
Petrolatum, to make	50 0

Label Apply gently to affected areas 2 to 3 times daily and bandage as directed. (Caution—do not use ammoniated mercury on large body areas because of possible systemic absorption.)

9 Scalp Ointment I.

Crude coal tar	0 5 1 5
Ammoniated mercury*	0·5 1 5
Petrolatum containing cholesterol derivative	
or Soft ointment of Prescription 6, to make	50 0

Label Rub gently on affected parts 2 to 4 times daily and bandage as directed.

Beware of possible sensitization to mercury

Hydrophilic petrolatum U.S.P XIV or one of the many products available under various trade names, *e g.*, Qualatum (Almay) Hydrosorb (Abbott), Polysorb (Fougera), etc.

10 Scalp Ointment II.

Salicylic acid	2·0 3 0
Precipitated sulphur	2 0 5·0
Liquid petrolatum	32·0
Lanolin	32·0
Petrolatum	32 0

Label As for prescription 9 (Do not use if mercury is given.)

APPENDIX B

FORMULARY

Prescriptions 1 to 27 by WITTEN and SULZBERGER,
28 and 29 by PETERKIN
30 to 35 by LOEWENTHAL.

PRESCRIPTIONS*

1 Solution of aluminium subacetate (Liq alumini subacetatis N F VI) or Burow s solution (Liq alumini acetatis N.F VI).

Label Dilute with 15 20 parts of water and use as cleanser or apply as wet poultices or dressings.

2. Boric acid (crystals or powder)

Label ½ to 1 teaspoonful to each tumblerful of hot water allow to cool and apply as cleansing solution or as wet compress.

(Remember—as the solution evaporates the concentration of the boric acid increases.)

3 *Potassium permanganate tablets 0 06 (gr i)*

Label Add 1 tablet to 1 2 pints of water (1 16 000 or 1 8,000 solution) Stir and *dissolve thoroughly* before using

4 Thiersch s solution (Liq borici salicylatis)

Boric acid	12·0
Salicylic acid	2·0
Distilled water to make	1 000 0

Label Apply undiluted as wet compresses.

5 Lubricating and softening oil.

Salicylic acid	2·4 4 8
Olive oil or Liquid petrolatum to make	240·0

Label For softening and removal of crusts, apply as directed

6 Softening and lubricating cream and soft ointment vehicle.

Liquid petrolatum	30·0
White wax	7 5
Distilled water	12·0
Sodium borate	0·225

Label Apply by gentle massage bandage on in thick layer if required

This preparation may be used also as a vehicle for antipruritics and many topical medicaments (except salicylic and other acids which will break down the emulsion).

*The National Formulas referred to in Prescriptions 1 7 are the National Formulas of U.S.A.

7 Mild dusting powder

Boric acid powder		
or Tannic acid		
or Bismuth subnitrate	1 3	3 0
Zinc oxide		
or Kaolin		
or Zinc stearate		50 0
Purified talc		50·0

Dispense in sifter top can.

Label Use freely as required.

8. Antiseptic ointment.

Neomycin sulphate	0·25	0·5
or Bacitracin	25,000 Units	
or Aureomycin hydrochloride	0·25	1 5
or Terramycin hydrochloride	0·25	1 5
Vioform powder	0·5	1 5
or Ammoniated mercury	0·5	1 5
Petrolatum, to make	50 0	

Label Apply gently to affected areas 2 to 3 times daily and bandage as directed (Caution—do not use ammoniated mercury on large body areas because of possible systemic absorption.)

9 Scalp Ointment I.

Crude coal tar	0·5	1 5
Ammoniated mercury*	0·5	1 5
Petrolatum containing cholesterol derivative		
or Soft ointment of Prescription 6, to make	50 0	

Label Rub gently on affected parts 2 to 4 times daily and bandage as directed.

Beware of possible sensitization to mercury

Hydrophilic petrolatum U.S.P XIV or one of the many products available under various trade names, *e g* Qualatum (Almay) Hydrosorb (Abbott), Polysorb (Fougera), etc.

10. Scalp Ointment II.

Salicylic acid	2·0	3·0
Precipitated sulphur	2·0	5·0
Liquid petrolatum	32·0	
Lanolin	32·0	
Petrolatum	32·0	

Label As for prescription 9 (Do not use if mercury is given.)

11 Scalp face and body ointment.

Crude coal tar 1·0 5·0
Simple ointment
or Zinc oxide ointment, to make 100·0

Label Apply and bandage as directed

12. Crude coal tar

Label Apply to affected areas in thick layer and powder over liberally with talcum. (Not to be used on extensive areas.)

13 Tar ointments and pastes.

Crude coal tar
or Naftalan
or Oil of cade 3·0 10·0
Zinc oxide ointment
or Lassar's paste
(zinc oxide paste) to make 100·0

Label Apply to affected areas 2 or more times daily

(Not to be used on extensive areas.)

14 Medicated vanishing type creams.

A Vioform cream (Ciba)
B Pragmatar (Smith, Kline & French)
C. Tarbonis (Tarbonis)
D Ammoniated mercury 1·0 3·0
Solution of coal tar 5·0 10·0
or Oil of Cade 3·0 10·0
in unscented "vanishing
cream" to make 100·0
(Stearic acid 14·0
Glycerin 14·0
Distilled water 70·85
Sodium borate 0·25
Potassium
carbonate 0·5)

(The Pharmaceutical Recipe Book 2nd ed Washington, D.C American Pharmaceutical Association [illegible] p [illegible])

Hydrophilic Ointment U.S.P XIV
or Neobase (Burroughs Wellcome)
Unibase (Parke Davis)
Emulsion base (Almay Schieffelin)
Cetophil (Texas Pharmacal)

(Many other similar bases are available on the market.)

Label Rub gently into affected areas several times daily

15 Shake lotion—mildly parasiticidal, anti-eczematous, soothing and drying.

Menthol	0·15	0·6
Phenol	0·15	0·3
*Red sulphide of mercury	1 2	2·4
Resorcinol	1 2	3·6
*Solution of coal tar	2·4	6·0
Calamine lotion, to make	120·0	

Dispense in wide-mouthed bottle.

Label Shake well and apply with paint brush or palm of hand on affected parts 3 to 4 times daily

*Can be omitted or included in any number and as desired.

Caution—when resorcinol or phenol are used for infants, over large body areas, signs of systemic poisoning, *e g.*, phenoluria, must be carefully watched for

16. Shake lotion for extremities, trunk neck, etc.

Zinc oxide	20 0
Talc (purified)	20 0
Glycerin	15 0
Distilled water or Distilled water and alcohol equal parts of each, to make	120·0

Label As in Prescription 15 (any or all adjuvants of Prescription 15 may be incorporated).

17 Soothing and drying lotion.

Solution of aluminium subacetate or Burow's solution	38·0
Purified talc	42·0
Zinc oxide	4 0
Glycerin	30 0
Lime water (liq calcii hydroxidi) to make	120·0

Label As in Prescription 15

(Any or all adjuvants of Prescription 15 may be incorporated.)

18 Calamine liniment (modified Pusey's liniment).

Tragacanth powder	4 0
Phenol	0 66
Glycerin	0 66
Prepared calamine	30 0
Zinc oxide	30·0
Olive oil	120 0
Distilled water to make	480 0

Label As in Prescription 15

(Any or all adjuvants of Prescription 15 may be incorporated.)

19 Medicated oils.

*Menthol	0·15	0·6
*Phenol	0·15	0·3
*Resorcinol	1 2	3 6
*Solution of coal tar	2·4	12·0
Eucerin emulsion (Duke) or Lubriderm (Texas Pharmacal) or similar oils containing cholesterol derivatives, to make	120·0	

Label Apply with palm of hand to affected areas 3 or more times daily

*Can be omitted or included in any number and as desired.

20 Protective paste

Zinc oxide	25·0
Purified talc	25·0
Petrolatum	50·0

Label Apply to affected areas twice daily

21 Sedative mixture

Chloral hydrate	1·0
or Phenobarbital sodium	0·12
Simple syrup to make	30·0

Label ½ teaspoonful in water 3 times daily

22. Phenobarbital 0 015 (¼gr).

23 Liquid "antihistaminics"—for sedative effects *

A. Elixir Benadryl	10 mg./ʒ (per teaspoonful)	
B Elixir Pyribenzamine	30 mg./ʒ	
C Chlortrimeton Elixir	4 mg./ʒ	"
D Trimeton Elixir	7 5 mg./ʒ	"
E. Syrup of Thephorin	10 mg./ʒ	
F Hydrallin Elixir	12 5 mg./ʒ	"

Label ½ to 1 teaspoonful 1 or more times daily

*Dosage will depend on tolerance Of course, it is understood that only in some cases may the "antihistaminics" have a sedative effect Responses differ from individual to individual and from "antihistaminic" to "antihistaminic." It is well known that the responses may vary from profound sedation to extreme excitement

24 Shake lotion—drying.

Menthol	0·6	1·2
Phenol	0·6	1·2
*Solution of coal tar	7·2	24·0
Resorcinol	4·8	12·0
Benzocaine	4·8	12·0
Zinc Oxide	40·0	
Talcum, purified	40·0	
Glycerin	30·0	
Alcohol		
Distilled water equal parts of each, to make	240·0	

Label Shake well and paint on affected part 3 or more times daily

Can be omitted or included in any number and as desired.

25 Shake lotion.

Ingredients indicated in Prescription 24	
Burow's solution (filtered)	38·0
Zinc oxide	42·0
Talcum, purified	42·0
Glycerin	42·0
Lime water to make	240·0

Label As Prescription 24

26. Emulsion.

Ingredients indicated in Prescription 24	
Calamine emulsion N.F VI to make	240·0

Label As Prescription 24

27 Ointment

Menthol	0·15
Phenol	0·15
Tannic acid	3·0
Benzocaine	3·0
Petrolatum, to make	60·0

Label Apply by gentle massage at night.

28. Lotion.

Hydrarg. perchlor		gr. ½	0·02
Acid. salicyl.	āā	ʒ j	2·0
Ol. ricini			
Ol. lavandul.		q.s.	
Spir meth. industr ad		℥ vj	100·0

Label Rub thoroughly into the scalp every night.

29 Ointment.

	Ung. Quinolor Co (Squibb)	
	Paraff. liq lev	aa pt. aeq

Label Rub in gently night and morning.

30 Paint.

Acid tannic.	2 5
Acid boric.	7 5
Glycerini	25·0
Aq dest. ad	240·0

Label Apply 2 or more times daily

31 Lotion.

Acid tannic	2 5
Acid boric.	7 5
Pulv zinci oxid	25·0
Glycerini	25·0
Aq dest. ad	240·0

Label Apply 2 or more times daily

32. *Ointment*

Acid. salicyl.	0·5
or Acid. boric	1 5
Vioform	1 5
Ol olivarum	10·0
Adipem lan hydr ad	50·0

Label Rub in well and wipe off twice daily

33 Paste.

Acid. salicyl		0·5
or Acid. boric		1 5
Vioform		1 5
Crude coal tar	1 5	3·0
Protective paste (No 20) ad		50 0

Label Apply under bandage every 24 hours.

34 Lotion

Vioform 3 per cent. in base of No 31

35 *To make a starch poultice* To 4 tablespoonsful of starch and one teaspoonful of boracic powder add sufficient cold water to make a thick cream While stirring add boiling water to make one pint. On cooling this sets in a jelly A layer of this jelly ¼ to ½ inch thick, is spread on linen and covered with a single layer of muslin or gauze. The poultice is applied with the muslin or gauze next to the skin and kept in position for 3 hours the poultice may be applied up to 4 times daily

INDEX OF AUTHORS

29 Ointment.

Ung Quinolor Co (Squibb)
Paraff. liq lev aa pt aeq

Label Rub in gently night and morning

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Acid boric	7 5
Glycerini	25·0
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or Acid boric.	1 5
Vioform	1 5
Crude coal tar	1 5 3·0
Protective paste (No 20) ad	50·0

Label Apply under bandage every 24 hours.

34 Lotion.

Vioform 3 per cent. in base of No 31

35 *To make a starch poultice* To 4 tablespoonsful of starch and one teaspoonful of boracic powder add sufficient cold water to make a thick cream. While stirring add boiling water to make one pint. On cooling this sets in a jelly A layer of this jelly $\frac{1}{4}$ to $\frac{1}{2}$ inch thick is spread on linen and covered with a single layer of muslin or gauze. The poultice is applied with the muslin or gauze next to the skin and kept in position for 3 hours the poultice may be applied up to 4 times daily

INDEX OF SUBJECTS